# Brain

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# BRAIN.

PART I., VOL. 37.

## THE CLINICAL ASPECTS OF SYPHILIS OF THE NERVOUS SYSTEM IN THE LIGHT OF THE WASSERMANN REACTION AND TREATMENT WITH NEOSALVARSAN.[1]

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[1] The substance of this work was given in the Schorstein Memorial Lectures, delivered at the London Hospital on March 19 and 26, 1914.



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THE following paper is the third of a series, which set forth the results of work carried out in conjunction with Dr. Fildes and Dr. McIntosh on the behaviour of the Wassermann reaction in diseases of the central nervous system. In the first communication laid before the International Congress of Medicine in August, 1913 [10], we dealt clinically and pathologically with the conception of "parasyphilis." The second paper by Fildes and McIntosh [3] described the technique of the Wassermann reaction employed by them, and the results obtained in cases of nervous disease of syphilitic origin.

We shall now discuss the clinical aspects of this work and attempt to substantiate certain conclusions we have reached concerning the classification of these syphilitic diseases, their prognosis and treatment.

In all these papers the numbers appended to the cases remain the same, so that wherever any one number appears it always refers to the same patient.

We are much indebted to Dr. R. Donald, who made all the cell-counts mentioned in this work. The method he uses of measured drops not only ensures great accuracy, but also provides permanent preparations [2].

## CHAPTER I.—INTRODUCTION.

Clinical medicine consists in the discrimination and classification during life of the phenomena evoked by pathological processes. The categories which emerge are spoken of as diseases. But the aim of such differentiation is to recognize the morbid process underlying the clinical manifestations for the purpose of treatment and prognosis; not infrequently, however, two conditions, apparently identical at the bedside, turn out to have a fundamentally different pathology. Thus, many patients with multiple syphilis of the nervous system are still

diagnosed as cases of disseminated sclerosis, a disease that stands in no relation to the *Spirochæta pallida*. Here the Wassermann test has enabled us to distinguish two diseases, often confused with one another, and this growth of knowledge has in turn been followed by closer clinical discrimination of signs and symptoms. On the other hand, two apparently different diseases, from the clinical aspect, may turn out to be based upon an identical morbid process. In such cases intermediate forms can be discovered between the two diseases, so that in some instances it may be impossible to say to which category a particular patient belongs. No two diseases could be more different, at first sight, than the classical forms of dementia paralytica and tabes dorsalis; and yet both are due to an identical pathological process attacking different parts of the central nervous system. A host of intermediate forms, necessitating the invention of the term "tabo-paresis," bear witness to the absence of a sharp line of demarcation between the two conditions, which depend for their clinical diversity solely on the anatomical incidence of the pathological process.

It has long been recognized that the manifestations of chronic syphilis of the nervous system cannot be separated into "diseases." In any one case symptoms and signs usually point to a simultaneous affection of both brain and spinal cord. We speak of encephalitis, myelitis, &c., according to the site of the principal lesion: but in the majority of instances careful clinical observation reveals signs pointing to affection of some other part of the nervous system. Thus a patient with myelitis may have pupils that do not react to light: hemiplegia may be accompanied by signs of a lesion of the spinal nerve-roots, or bulbar symptoms may be associated with a disturbance of micturition. The morbid process underlying all the conditions is the same; they are different manifestations of the same disease.

Until recently, however, it was universally held that the pathological process, underlying these cases of chronic syphilis, differed fundamentally from that in "parasyphilis" of the nervous system. Fournier invented the term to signify a condition which required syphilis as an antecedent, but was not itself an active manifestation of the syphilitic virus. This conception he based on the refractory nature of "parasyphilis" to treatment with anti-syphilitic remedies.

When, however, Noguchi demonstrated the presence of the *Spirochæta pallida* in the brain of patients who had died from dementia paralytica, the first half of Fournier's contention fell to the ground. Moreover McIntosh and Fildes have proved that little, if any, arsenic enters

the substance of the central nervous system after the injection of salvarsan or neosalvarsan, and so gave a more probable explanation of the insusceptibility of "parasyphilis" to such remedies. "Parasyphilis" is refractory to treatment, not because it depends on a different pathological process, but because the virus is active in parts that are not reached by the drug in effective doses.

The difference between chronic syphilis of the nervous system and "parasyphilis" is not a difference of morbid process but of anatomical situation and chemical permeability; for the deeper the virus lies in the substance of the central nervous system, the less will it be reached by treatment which readily acts on the same process affecting vessels and meninges.

But although "parasyphilis" of the nervous system is at bottom simply another manifestation of syphilitic spirochætosis, we believe that the conditions, classed under this head, require a previous sensitization of some part or parts of the central nervous system. This antecedent preparation of the tissues is also required for the formation of a gumma, and both "gummatosis" and "parasyphilis" are manifestations of the activity of the spirochæte in tissues that have become hypersensitive during previous stages of the infection. The difference between them lies in the tissues attacked. In the one case it is the meninges and vessels, in the other the reaction to the spirochæte occurs in the neuroglia and essential nerve-structures.

It is universally recognized that the reaction which forms what we call a gumma is out of all proportion to the number of spirochætes that can be discovered within it. In the same way we suspect that the difference between the clinical course of cases of "parasyphilis" and of the acuter forms of cerebrospinal syphilis lies in the extent to which the central nervous system has become hypersensitive.

We shall show that it is quite impossible, in many cases, to diagnose the difference between syphilitic encephalitis and dementia paralytica without observing the effect of treatment and the changes it produces in the Wassermann reaction. In the same way syphilitic meningomyelitis may simulate tabes dorsalis, or may evoke signs and symptoms that closely resemble amyotrophic lateral sclerosis.

All these categories of disease have been destroyed by recognition that the pathological process is the same in nature though different in the site of its activity and the condition of the tissues on which it acts. We shall attempt in this paper to show how a reconsideration of the clinical signs and symptoms, aided by the Wassermann reaction,

can lead us from this chaos to diagnosis of the site of the lesion and to recognition of the probable behaviour of the disease.

First of all, however, it will be necessary to consider nomenclature in the light of these conceptions of syphilitic disease of the nervous system. We cannot hope to obtain a post-mortem examination in any but a minute proportion of the patients under observation; for many recover, and most of those who die drift off into Asylums and Workhouse Infirmaries where they excite little interest.

All names given to such diseased conditions must correspond to clinically demonstrable states. If the signs point to affection of a series of posterior nerve-roots some meningitis must be present and in the same way a sudden hemiplegia signifies in most cases vascular disease. Similarly loss of recognition of posture and want of appreciation of the vibrating tuning-fork indicate destruction of the posterior columns, which, if widespread, show that a lesion is situated in the substance of the spinal cord.

Then, again, by watching the behaviour of the disease after intravenous injections of neosalvarsan or allied drugs, we are able to recognize if it is amenable to treatment or not. When rapid improvement occurs not only in symptoms and signs, but also in the Wassermann reaction in the cerebrospinal fluid, we can be certain that the lesion is situated in parts, such as the meninges and vessels, easily reached by a drug circulating in the blood. But no improvement in the clinical condition, accompanied by a positive Wassermann reaction in the cerebrospinal fluid, unchanged over months or years, points to an affection of the deeper structures of the nervous system, which are nourished by fluids not reached effectively by the arsenical compounds employed according to the present methods.

All nomenclature must, for the present, depend on the interpretation of phenomena which are clinically recognizable, and must not be based on hypothetical pathological states. Thus "tertiary" or "gummatous" must not be applied to clinical conditions, and it will be wiser to get rid altogether of the word "parasyphilis," because it conveys a false pathological conception and gives no indication of the form or nature of the clinical manifestations in any case to which it may be applied.

We propose, therefore, to divide cases of syphilitic disease of the central nervous system into those of syphilis meningo-vascularis and syphilis centralis. The meaning of the first name is obvious, for in many cases we know from clinical observation that the meninges and vessels must be affected. Syphilis centralis was chosen to include all

those cases where the degeneration of nerve-tracts or nuclei shows that the lesion must lie within the structure of the nervous system itself. This category includes "parasyphilis," used in the strict sense for those forms of the disease which are not materially influenced by our present methods of anti-syphilitic treatment. The name syphilis centralis was selected in preference to "parenchymatous" syphilis, favoured by so many speakers at the International Medical Congress, because we wish to lay stress on the reaction to the syphilitic virus of both the neuroglia and essential nerve structures (McIntosh, Fildes, Head and Fearnsides [10]). We are not at variance in any way with those who speak of "parenchymatous" syphilis, but believe the term syphilis centralis is less likely to lead, in the future, to the erroneous view that the nerve elements alone react in these cases to the toxic action of the spirochæte.

## Chapter II.—The History of Infection.

Before the coming of the Wassermann reaction it was impossible to be certain that the patient had been infected in the past without a history of chancre, rash, sore throat, or other signs of syphilis. Every physician recognized that undoubted late manifestations, such as tertiary lesions or tabes dorsalis, might appear in persons who honestly denied all knowledge of infection. This cast an uncomfortable shadow of doubt over all diagnosis in chronic diseases of the nervous system, which has been dispersed by the employment of the quantitative estimation of the strength of the Wassermann reaction in the serum and cerebrospinal fluid. It will be well, therefore, to review this question in the light of the histories we have obtained in the patients investigated for this research.

But first of all we wish to endorse the experience of Erb, and later of Nonne, that conscious denial of infection is uncommon, provided the patient is questioned quietly and with reasonable precautions. It is absurd to suppose that a man will be truthful if he is questioned in a public ward before students and nurses, especially when he may himself have some doubt as to his answer. Again we are not likely to obtain a detailed account of his infection from a patient with dementia paralytica or other brain disease which destroys the memory. But, if after his confidence has been gained the necessary questions are asked in a kindly and business-like manner, we have always discovered a remarkable desire on the part of the sane patient to help us to determine the date of infection and its sequelæ.

On the other hand, in a woman it is neither possible nor desirable, in many cases, to probe the history of infection; we must rest satisfied with a positive Wassermann reaction and a history of illness or a series of miscarriages which occupied some period of her life.

Out of forty-seven males of the hospital class suffering from active syphilis of the nervous system, who were investigated for this research, thirty-nine admitted some sign of syphilitic infection and could give its approximate date. Four patients acknowledged gonorrhœa only, and four admitted exposure but denied all venereal disease.

Let us next consider the history of 70 patients with classical tabes dorsalis; of these 48 were seen by one of us in private practice and 22 were of the hospital class and appear in the records of this research. Amongst these 70 patients, 8 denied all venereal disease but confessed to frequent exposure, while 16 admitted gonorrhœa but denied all syphilitic infection and showed no local scar.

Thus amongst 117 males, all of whom demonstrably suffered from syphilis of the nervous system, 12 denied all venereal disease (10 per cent).; these are the cases of "syphilis d'emblée," where the infection occurs without local reaction. At the same time the general infection was so wanting in virulence, or the reaction of the body was so effective, that it was apparently not followed by such manifestations as a rash, sore throats, or fall of hair.

A more important group from the clinical point of view is formed by the 20 cases (17 per cent.) where the syphilitic infection ran its course under cover of a gonorrhœa. It would seem as if, in some persons, the gonorrhœal inflammation had permitted general infection with the spirochæte to occur without the obvious formation of a specific local reaction.

## Chapter III.—Early Symptoms and Signs of Cerebrospinal Syphilis.

To clinicians who have not interested themselves particularly in neurology a diagnosis of syphilis of the nervous system evokes definite clinical pictures, as, for instance, that of a "myelitis." But such gross diseases are usually the final stage of a process which has previously manifested itself in a host of minor conditions that usually pass unrecognized. It is, however, in this early stage that the disease is amenable to treatment; for the symptoms and most of the signs which accompany a "myelitis" are due to secondary destructive processes, such

as hæmorrhage, and cannot be materially affected by anti-syphilitic remedies.

This chapter will therefore be devoted to a consideration of the early symptoms and signs of cerebrospinal syphilis. We have excluded all cases that would be usually called "parasyphilis," such as classical examples of tabes dorsalis, because we hope to show how frequently these disturbances of function anticipate the better known and graver signs of cerebrospinal syphilis. Everyone is familiar with the occurrence of root-lesions in the course of tabes dorsalis, but they are less often recognized as the precursor of syphilitic disease of the spinal cord and its membranes.

Early diagnosis means the certain recognition, before the onset of grave destructive changes, that the more or less trivial signs and the symptoms of which the patient complains are due to active syphilitic spirochætosis. A few years ago the acute clinician might suspect the true origin of the headaches, shivering attacks, malaise, pupillary abnormalities or curious radicular changes in sensation; but now the perfection of the Wassermann reaction has converted such a hypothetical diagnosis into a certain one. Moreover, the fact that we can be sure, in many cases, of the syphilitic origin of these morbid states has made it possible to study them with greater precision, and to obtain a clearer clinical view of the conditions under which they appear and the significance of their occurrence.

### § 1.—*Changes in Personality and Aptitude.*

One of the earliest alterations produced by the activity of cerebrospinal syphilis is a change for the worse in character and personality. A skilled workman ceases to be worth his high wages. The steward of a golf course found that he could not remember the many little details necessary to the success of his day's work (No. 3, p. 34). A Jewish baker "lost all his manners at home and could not be trusted to carry out completely the processes of the bakehouse." A fireman on the railway lost his job because he used to fall asleep during his hours of duty (No. 59, p. 37). In one case, where we previously knew the patient, we readmitted him to hospital solely on a change in his manner, greatly to his own surprise; the Wassermann reaction, and subsequent closer clinical examination in the wards, justified our diagnosis that he had relapsed. The patients who formed the material of our research were solely those who came to a General

Hospital, and did not include the insane. The mental changes we were able to observe appeared in the course of some gross physical manifestation of syphilis of the central nervous system. In some cases they passed away as the graver signs developed and, in most instances, they yielded rapidly to treatment. Though slight they were very common amongst the class of patients with whom we have had to deal.

Attention and the power of concentration commonly suffer and the patient can no longer carry through a full day's work; moreover he is liable to make mistakes in details with which he has long been familiar. Memory for recent events becomes uncertain and capricious, because he cannot concentrate his attention upon them at the time with sufficient intensity.

These patients frequently become highly emotional and untrustworthy in their social relations. That balance between emotion and reason, which forms the basis of individual personality, is disturbed. They are "not themselves" and become uncertain and hesitating in action.

In this condition they are commonly thought to suffer from neurasthenia, and the organic basis for the symptoms is not suspected until too late for effective treatment.

*A Case of Supposed Neurasthenia with a Negative Wassermann Reaction in the Serum, but a Positive Reaction and an Increase of Cells in the Cerebrospinal Fluid.*

*Case* 123.—G. P., male, single, clerk: born in 1885. In November, 1910, at the age of 25, he contracted syphilis and suffered from a chancre for which he was treated with mercurial pills from December, 1910, to October, 1911.

Twelve months after infection, in November, 1911, a crop of warty spots appeared on his forehead, face and neck, and persisted for fourteen days. Some time before Christmas, 1911, he developed a weeping eczema on the legs, forearms and dorsum of his hands, and in December, 1911, his tongue became ulcerated. He then attended the skin department of the London Hospital under the care of Dr. J. H. Sequeira, and was injected with two doses of 0·6 grm. of salvarsan. Under this treatment the ulceration of his tongue healed rapidly; the eczema, however, persisted unchanged. During the months from March to October, 1912, except for the eczema, he remained in good health.

Within two years of infection, however, he began to complain of left-sided frontal headache, and in November, 1912, was sent to Dr. Fildes and Dr. McIntosh for further examination of the blood and cerebrospinal fluid. On November 25, 1912, the Wassermann reaction was $\frac{\text{serum } 0.0.0.0.0.}{\text{c.s.f. } 4.4.1.0.0.}$ and the cells in the cerebrospinal fluid were 85 per cubic millimetre. And yet at this time the most careful examination in the Hospital failed to reveal any signs of disease of the central nervous system.

He did not come under our observation between November 29, 1912, and May, 1913. But when he was again admitted on May 28, 1913, he had become neurasthenic, introspective and less rational in his habits: at the same time his capacity for business had failed.

He complained that on May 18 he had caught a "chill," which was followed by acute pain in the left chest "around the heart." This pain was followed by shortness of breath, but he did not suffer with a cough and there was no expectoration. On examination in the Hospital (May 28, 1913) movement was defective at the base of the left half of the chest, the percussion note was impaired and the air entry defective. The heart was not displaced. X-ray examination of the chest showed some doubtful obscuring of the left half of the diaphragm. The lungs themselves were completely unaffected. We were thus left in doubt as to whether the pain was of root origin or whether it was due to a pleurisy at the left base.

Mentally the patient was very unstable: he was emotional and irritable: he resented questions and gave illogical answers. No hallucinations or delusions were present. He slept badly and complained of severe general headaches, referred chiefly to the occipital region and the back of the neck.

The fundi appeared natural. All ocular movements were well carried out. The pupils reacted well to light and accommodation. Motion was unaffected. No disturbance of sensation could be detected. The reflexes, sphincters and spine were unaffected.

No abnormal signs were detected in the heart or abdomen. The urine contained neither albumen nor sugar.

On June 6, 1913, the Wassermann reaction was $\frac{\text{serum}\ 4.4.4.4.2.}{\text{cs.f.}\quad 4.4.4.4.3.}$ and the cells numbered 90 per cubic millimetre.

He was injected on June 6, 1913, with 0·6 grm. of neosalvarsan, on June 12, on June 18, on June 23, and on July 26 with 0·9 grm.

On August 13, 1913, the Wassermann reaction was $\frac{\text{serum}\ 4.3.2.0.0.}{\text{cs.f.}\quad 4.4.4.0.0.}$ and the cells were 3 per cubic millimetre: he was then injected again with 0·9 grm. of neosalvarsan.

Under this treatment his mental state improved rapidly and the pains in his chest disappeared: by the end of September, 1913, he would have passed both mentally and physically as completely normal.

On September 24 and on November 15, he was injected with 0·9 grm. of neosalvarsan.

On November 15, 1913, the Wassermann reaction in the serum was again completely negative.

On January 28, 1914, the Wassermann reaction was $\frac{\text{serum}\ 0.0.0.0.0.}{\text{cs.f.}\quad 4.2.0.0.0.}$ and the cells numbered 5 per cubic millimetre.

Occasionally, however, the first intimation that syphilis has attacked the central nervous system is a slowly increasing dementia. The

patient "sits about" listlessly, unwilling to begin either work or play. He cannot remember when or where he was born, his age, or the details of his recent life. He sleeps the greater part of the day and resents being roused: occasionally the condition may resemble that of dementia præcox, but none of our patients have shown true negativism (cf. Plaut [18], p. 55).

*An Instance of the Cerebral Form of Cerebrospinal Syphilis.*

*Case* 284.—R. M., male, married, clerk; born 1887. In 1905, at the age of 18, this patient contracted syphilis and suffered from a "running which lasted a few weeks only," followed by a succession of bad throats, but no rash. He was treated for gonorrhœa only. Two years later he began to have attacks of "rheumatic pains" in the legs; these passed away without treatment. In 1907 he married. After marriage he remained well until the beginning of 1913. His wife has miscarried three times and there are no living children.

About April, 1913, ten months before he first came under observation, his employers noticed that he had become less trustworthy and less certain in business, and his wife stated that about the same time he became more irritable at home.

On December 17, 1913, whilst adding up the accounts in the office, he had a seizure, "he came over giddy and felt numb all down the left side": the attack itself lasted about ten minutes. Afterwards the left side of his face was drawn up and his speech altered. He then began to suffer from intense generalized headaches; these would come on in attacks which always seemed to affect the left half of the body and made him unable to hold small objects in his left hand. One day, early in January, 1914, whilst walking in the street, he had a second seizure. A sudden pain seemed to start in the left forearm, shoot into the left hand and then pass into the left axilla. The pain made him feel giddy, but he did not actually fall. He was helped to a tram and went home to bed. After the attack the whole of the left half of the body, face, arm, leg and trunk seemed numb, and the left leg became weak. He continued at work until February 20, 1914. On that day, whilst watching a gymnastic exhibition, he became very excited and had a third seizure, accompanied again by much giddiness, and followed by a feeling of weakness and numbness in the left half of the body, face and extremities. After the first seizure he had experienced at various times some difficulty in passing urine; either he had had to wait after desire came or else he had had to hurry to avoid wetting himself. Memory and aptitude in business failed. After December, 1913, he could no longer be trusted to do his work up to the old standard, and he found difficulty with his accounts. He became depressed and at home was restless and irritable. The headaches became extremely troublesome and would last in attacks over a period of days. He also complained of much giddiness with nausea and feelings of inability to concentrate at work. From time to time he had been subject to shooting pains in the occipital region and more especially

in the back of the neck. He had slept badly, but at the same time had often fallen asleep when at his work. At nights "sleep was disturbed and never seemed to rest me." When walking the left leg felt "dead and useless."

He first came under observation on February 23, 1914. No abnormality was discovered in the heart, lungs, abdomen, or urine.

The patient was a well-informed, intelligent man. Attention was fleeting and erratic. He disliked all restraint and was restless and irritable over the restrictions of hospital routine. Memory for recent events was extremely defective, but was little impaired for those of long ago. Writing was unsteady and the letters were badly formed. Speech was definitely affected; the syllables were slurred and the words badly pronounced.

He complained of a throbbing headache in the frontal region and the occiput was tender to pressure. The headache led to a feeling of sickness, and he vomited on several occasions before treatment was begun. Vision was unimpaired, and the visual fields were of normal dimensions. The optic discs appeared natural but the veins of the fundus oculi were engorged. The other special senses were unaffected.

The pupils were large, reacted sluggishly to light but dilated on continued exposure; they reacted briskly to accommodation and convergence. The face showed little expression. The tongue was protruded straight, but could not be held steadily. Otherwise, no abnormalities were discovered in the territory of the cranial nerves.

The gait was rolling. Fine movements of the left hand were performed clumsily and the fingers on each side were badly aligned. No local muscular atrophy and no changes in muscular tone were discovered.

He complained of a curious numb feeling in the left half of the body, but no gross loss of sensibility was discovered on testing.

The knee-jerks and ankle-jerks were brisk and equal on the two sides. Ankle-clonus was not present. Both plantar responses were flexor. The abdominal reflexes were obtained with difficulty on both sides.

He complained of some difficulty in holding and in passing urine, and not infrequently wetted the bed.

On February 25, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.}{\text{c.s.f. } 4.4.4.4.0.}$ and the cells numbered 65 per cubic millimetre. He was injected with 0·45 grm. of neosalvarsan on February 27, 1914, and with a similar dose on March 2. On March 4, and on March 7, 0·9 grm. of neosalvarsan were given.

By April 30, 1914, the patient returned to work mentally and physically a normal man.

### § 2.—*Disturbance of Sleep.*

All forms of disturbance of sleep may appear among the early symptoms of cerebrospinal syphilis. Occasionally the patient falls asleep on the most inopportune occasions, but more usually he becomes

sleepless. Insomnia is a common accompaniment of that state of emotional irritability mistaken for neurasthenia.

But in some cases the patient tends to fall into a "half-conscious sort of state" even in the day. He cannot rouse himself to take in what is going on around him. At night this condition takes the form of a mild delirium; thoughts race through his head and he may fall into a state resembling a mild confusional psychosis (Heubner [6], Oppenheim [16], p. 50, Plaut [18], p. 93).

In one case the patient complained that she was not "herself"; when it was dark she would see "strange sights" and thought "God was talking with her." "Horrible dreams," noises heard at night and even "ghosts" may be manifestations of this nocturnal state (No. 3, p. 34).

Occasionally the patient complains that the headache, so common in cerebrospinal syphilis, keeps him from sleep, and that he then sees "terrible things"; he lies awake full of fear and anxiety.

Such nocturnal psychoses are commoner than is usually supposed amongst sane patients suffering from syphilis of the central nervous system. They are obviously nothing but milder forms of that confusional insanity, accompanied by hallucinations, frequently associated with severe syphilitic encephalitis (Plaut [18], p. 27 *et seq.*).

*Acute Syphilitic Encephalitis with Profound Mental Changes. Death; Autopsy.*

*Case* 183.—S. B., female, married; born 1880. This patient was admitted to the London Hospital, under the care of Dr. Russell Andrews, on May 8, was transferred to the care of Dr. Head on May 23, and died on May 30, 1913.

There was no definite history of any syphilitic infection, but her husband's serum gave a positive Wassermann reaction (4.4.4.1.0).

In 1898, at the age of 18, she married her first husband, who died, aged 20, three weeks after marriage, from "abscess on the brain." She then courted her second husband for three years, and married him in 1903; by him she was pregnant six times (1) a girl, born August, 1904; (2) a girl, born 1907; (3) a stillbirth at the eighth month; (4) a boy, born 1908; (5) a girl, born 1909; and (6) a child born in Hospital on May 8, 1913; five healthy children survived her death.

Since her second marriage she had always been subject to "fainting attacks," often two or three in the twenty-four hours, at any time of night or day; she complained of "feeling faint" and of "losing herself" momentarily in these attacks. With this exception she had had no illness since 1903, and all her five previous pregnancies had been uneventful.

In June, 1912, almost a year before her death, her memory was noticed to be failing: she made no complaint, but her friends said that she was "no longer herself." Shortly after this she would complain of hearing noises in the dark, and at night, and interpreted them as "bells" or "God talking with me." She also complained of seeing strange sights of various sorts in her own kitchen. From time to time between June and December, 1912, these hallucinations had worried her and her husband said that at times she had behaved "as if out of her mind."

In December, 1912, she discovered that she was again pregnant. About this time her husband lost his employment, and immediately his wife's mental condition seemed to improve. During the months between December, 1912, and April, 1913, her condition altered little, but the fainting attacks came on more frequently.

On May 6, 1913, she developed "epileptiform attacks," and was admitted to the Maternity Wards as "eclampsia." Before admission she had five of these attacks and became "dazed and funny." On admission labour had begun; a Champetier de Ribes' bag was inserted, and a healthy child, weighing 5 lb., showing no signs of congenital syphilis, was delivered six hours later. An examination of the urine on admission showed the presence of a cloud of albumen, and a positive reaction with ferric chloride, but no alteration in the ammonia-urea nitrogen ratio. The puerperium was uneventful, except for the fact that the patient at times talked irrationally: she complained of seeing strange objects in the ward after dusk and hearing noises "from under her bed." Slight pyrexia to 99·8 F. (37·6° C.) followed delivery, but the lochia were normal.

On May 18, 1913, ten days after delivery, the patient was allowed to get up. She then became subject to attacks of exaltation and of weeping. Examination at this stage showed that, though the pupils were of normal size, their reaction to light was extremely sluggish.

On May 23, 1913, she was transferred to the care of Dr. Head. At this time she complained of hearing voices, usually the voice of God telling her of her many misdeeds, or of the devil telling her to commit wrong. She said that the voices were all around her and constantly at work. Her emotional state varied, at one time she would laugh immoderately, at others she would be moved to tears.

Her memory was extremely bad: she could give no connected account of herself or of her previous health and habits. Speech was thick and slow and articulation was defective, syllables being missed out or badly slurred. She could not write and would not read either aloud or to herself.

She complained of no headache, and whilst under observation did not vomit.

Shortly after transfer to the medical ward she began to show attacks in which she clutched the bed-clothes or moved her arms to and fro wildly.

The special senses were unaffected, and the disc and fundus on both sides appeared healthy.

Ocular movements were well carried out. The pupils were equal in size, but reacted badly on exposure to light: the reaction obtained was ill-sustained. The left half of the face appeared flatter than the right, and in the lower half moved badly on volition. The tongue was protruded straight, but could not be held steadily. There was no tremor of the lips. The palate and larynx were unaffected.

No muscular paralysis was discovered and all movements could be carried out at will.

Owing to her mental state sensation could not be tested.

The tendon reflexes were all extremely brisk: ankle-clonus was not obtained, and the plantar responses were of the flexor type.

The sphincters and spine were unaffected.

On May 24 and 25 the condition altered but little. On the night of May 25 to 26, after a period of excessive restlessness, she had five epileptiform attacks accompanied by general convulsions, cyanosis and loss of consciousness.

On the morning of the 26th she was dull, somnolent, stuporous and subconscious, and could be roused only partially. The temperature rose to 103° F. (39·3° C.), and the rate of the pulse to 150 beats per minute, whilst respirations became rapid and sighing, 40 per minute. On examination on this day she was seen to have a divergent squint of the right eye.

During the next three days, the 27th, 28th and 29th, she remained dull and drowsy. She wasted rapidly, her orbits became sunken, bilateral purulent conjunctivitis and incontinence of urine set in. The temperature remained between 102° to 103° F. (38·5° to 39·3° C.), the rate of the pulse 112 to 130 and the respirations 44. Examination showed the persistence of the squint, but no complete paralysis of any eye muscle. The reflexes remained unaltered.

At 4 p.m. on May 29, 0·9 grm. of neosalvarsan were injected intravenously: the temperature and the rate of the pulse immediately fell and six hours later the general condition had apparently greatly improved. Twelve hours after the injection, however, the patient had an attack with cyanosis lasting fifteen minutes. She then seemed to recover and at 6 a.m. ate a good breakfast. At 7 a.m., however, respiratory failure again developed and seventy-five minutes later, despite the free administration of stimulants, she died.

On May 27, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f.} \quad 4.4.4.4.4.}$ and the cells numbered 33 per cubic millimetre.

## § 3.—*Headache.*

All clinicians have laid stress on the frequency with which headache appears amongst the first symptoms of syphilis of the central nervous system; but too much emphasis has been laid on its nocturnal occurrence.

It is usually severe, paroxysmal, and lasts for several hours. Some patients speak of it as "maddening." In one instance it appeared three or four times a week in the evening, and lasted for twelve hours. The whole scalp may become tender so that the patient cannot wear a hard hat (No. 262, p. 62).

We have seen no patient in whom this headache was strictly and constantly localized to a particular portion of the head, and if tenderness is present it is usually widespread. Localized tenderness confined to a comparatively small area should lead to a careful search for a gumma of the skull or its coverings. In cases where such a gumma is present, for instance in the temporal region, a fan-shaped area of superficial tenderness can usually be discovered; this is wider towards the vertex and converges towards the point in the temporal region at which the gummatous thickening can usually be felt. This is due to irritation of the small nerve-trunks which spread out towards the periphery after passing through the area of gummatous inflammation. On the forehead a gumma causes a similar area of tenderness which extends directly backwards from the point at which it is situated.

Occasionally the headache of cerebrospinal syphilis is accompanied by nausea which may culminate in vomiting. This leads to much difficulty in diagnosis, and if optic neuritis is present the case may be thought to be one of cerebral tumour. In fact, the differential diagnosis between the two conditions, if the serum gives a positive Wassermann reaction and the cerebrospinal fluid a negative, may be one of extreme difficulty.

*Headache, Vomiting and Optic Neuritis Three Years after Infection with Syphilis.*

*Case* 122.—J. P., female, single, skirt hand; born 1893. This patient was infected with syphilis at Christmas, 1909, just before she was 17, and shortly afterwards began to suffer with headaches and recurrent sore throats. In August, 1910, she gave birth to a child, which died seven weeks later of congenital syphilis and wasting. Whilst pregnant she was treated for some time with mercury by the mouth.

From August, 1910, until August, 1912, she remained in fairly good health.

About August, 1912, she began to suffer from recurrent attacks of universal headache, usually worst in the morning and affecting chiefly the frontal region and upper portions of the face; the pains were described as "throbbing." When the headache was severe the scalp became tender. She kept at work until November, 1912, but gradually became more and more "tired and drowsy." The headaches then led to a continual feeling of sickness, but about the middle

of November first caused actual vomiting. She would vomit nearly every morning, and this at first relieved her headache.

On the morning of December 2, 1912, she awoke to find that her right eye had "turned in," and from that time until her admission on January 4, 1913, everything appeared "double." Vision gradually failed and all objects appeared misty and distorted.

Between August, 1912, and the date of her admission her menses had ceased, but she was not pregnant. On admission to the London Hospital in January, 1913, the patient was seen to be a small, undersized, pale, anæmic girl. The temperature was slightly raised and oscillated between 98·8° F. and 99·4° F. [about 37·4° C.]. The rate of the pulse was rapid and usually about 100 beats per minute. The lymphatic glands in the posterior triangle of the neck on both sides and the epitrochlear glands were definitely enlarged. No rash was present and the tonsils and pharynx appeared healthy. No abnormal signs were discovered in the heart, lungs, abdomen or urine.

Mentally she was dull, stupid and slow. Speech was little affected. She complained of intense generalized headaches with pressure tenderness of the skull in the occipital and frontal regions. As an in-patient she complained of no nausea and she did not vomit.

Vision on both sides was defective, more especially for form: the patient complained that all outlines were distorted. Optic neuritis of moderate severity was present; the vessels were full and tortuous, the lamina cribrosa filled in and the edges of the disc blurred. About 3 D. of swelling was measured in each eye. Hearing, smell and taste were unaffected.

The patient complained of diplopia. On examination, all movements could be carried out, but the axes of the two eyes did not move together so as to produce binocular vision. The right eye moved outwards more sluggishly than the left. No ptosis or nystagmus was present. The left pupil was wider than the right; both reacted sluggishly to light, but readily to accommodation. The face was flat and expressionless. The tongue could not be held steadily. The cranial nerves were otherwise unaffected. There was no interference with motion, sensation or control of the sphincters.

The knee-jerks were readily elicited, ankle-clonus was not present, the abdominal reflexes were obtained and both plantar reflexes gave a flexor response.

On January 8, 1913, the Wassermann reaction was $\frac{\text{serum}\ 4\,4.4.4.4.}{\text{cs.f.}\quad 0.0.0.0.0.}$ and the cells numbered 10 per cubic millimetre.

On January 10, January 17 and January 23, 1913, intravenous injections of 0·9 grm. of neosalvarsan were administered.

After treatment the anæmia disappeared, the glandular enlargement subsided and the mental condition of the patient improved. Vision became almost normal and seven days after the first injection the diplopia had passed away; from this time the headaches ceased.

This headache may exist for a considerable time as an isolated

manifestation, and we believe that in cases where the patient has been treated with success the reappearance of the characteristic headache is an invaluable sign of a "relapse."

### § 4.—*Shivering Attacks.*

Several instances have come under our notice in which shivering attacks, with or without fever, formed the earliest manifestation of syphilis of the central nervous system.

In the following case no cause could be found in the urinary tract, the lungs, or in any other organ for the shivering and malaise; for, although the first attack was accompanied by swelling of one testicle, this complication was not present in the severer attacks which followed. It is interesting to notice that symptoms of irritation of posterior roots finally made their appearance.

*Recurrent Attacks of Shivering with Pyrexia, forming the earliest sign of Syphilis of the Central Nervous System.*

*Case* 63.—W. G., male, married, railway shunter; born 1878. In 1895, at the age of 17, this patient caught syphilis and suffered from a chancre and rash; he was treated for six weeks.

Thirteen years later, about Christmas, 1908, he began to complain of "shivering attacks," aching pains in the back, loss of weight, depression and irritability. In August, 1909, he was admitted to the London Hospital complaining of these symptoms, and was found to have a gumma of the left testicle. He was treated with 15 inunctions of mercury, and large doses of potassium iodide, and three weeks later was discharged, free from all subjective manifestations.

He then remained well until August, 1911, when the shivering attacks and feelings of malaise returned.

He was readmitted in April, 1912, and again treated with inunctions of mercury. On admission the temperature oscillated between 100° F. and 101° F. (37·8° C. to 38·4° C.), he complained of shivering attacks and much headache, but the only definite sign discovered was tenderness of the scalp on pressure; and yet on April 3, 1912, the Wassermann reaction was $\frac{\text{serum}\ \ 4.4.4.4.4.}{\text{cs.f.}\quad\ 0.0.0.0.0.}$, whilst the cells numbered 112 per cubic millimetre.

After this treatment he remained well until Christmas, 1913; then he began to suffer again from shivering attacks, headache, "rheumatic pains" in the arms, legs and body and somnolence.

On March 2, 1914, he was readmitted with a temperature of 100° F. to 101° F. (37·8° C. to 38·4° C.), which fell after an injection with 0·9 grm. of neosalvarsan. The mental state, special senses, cranial nerves, motion, reflexes and sphincters were completely unaffected. He complained of headache, which was

accompanied by pressure and percussion tenderness of the skull. Areas of tenderness were found over the outer aspect of the right leg below the knee, along the inner side of right arm and armpit; a band of tenderness was present on both halves of the abdomen below the level of the umbilicus. These areas gave the usual excessive reactions to the dragged point of the pin and to extremes of heat and cold; but no definite loss of sensibility could be discovered.

On March 4, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f.} \quad 0.0.0.0.0.}$ and the cells numbered 117 per cubic millimetre.

He was injected with 0·9 grm. of neosalvarsan on March 5, March 8, and March 11, 1914.

After this treatment the shivering attacks ceased and the areas of tenderness could no longer be determined.

With this case it is well to compare No. 149, p. 58, where the shivering attacks were associated with defective reaction of the pupils and polyuria.

### § 5.—*Root Lesions.*

Neuralgic pains in various parts of the body are recognized as an early symptom of syphilis of the nervous system, but the signs which point to the radicular origin of these pains have not been so generally appreciated.

As soon as a group of muscles begin to waste, the patient consults his doctor; but he does not trouble to complain of a patch of defective sensibility. Yet it is of extreme importance to recognize the significance of these localized sensory symptoms and signs because, in one form or another, they are far commoner than affections of the motor nerve-roots. Moreover, they reveal the changes, occurring within the spinal canal, at a stage when the syphilitic process is amenable to treatment, and has not yet caused irreparable secondary damage.

Our first example is a woman who showed both muscular wasting and loss of sensation in the left lower extremity. The muscles in the upper part of the front of the thigh and the whole of the extensor group were wasted, and there was some loss of power in the flexors and extensors of the left leg.

This muscular wasting was associated with complete loss of sensation to prick, heat and cold over the area shown on fig. 1; the loss of sensibility to cotton-wool was not so clearly defined, and was everywhere somewhat less extensive. This is characteristic of a lesion of the posterior root-fibres, either without or within the spinal cord, before the impulses have undergone regrouping at the first synaptic junction

(Head and Sherren [5]). The sensory loss corresponded to destruction of at least the first and second lumbar roots, whilst the motor disturbance pointed to an even more extensive lesion.

*A Case of Disturbance of Motor and Sensory Nerve-roots. Recovery of Power and Disappearance of the Wassermann Reaction in the Cerebrospinal Fluid in consequence of Treatment.*

*Case* 60.—Ada G., female, married; born 1876. This patient was married in 1905 at the age of 29. Shortly after marriage her health failed and eight months later she miscarried of a six and half months' fœtus which was peeling; the second child, Jessie G. (No. 61), born in 1906, gives a positive Wassermann reaction in the serum and shows a monoplegia of the right arm: the third

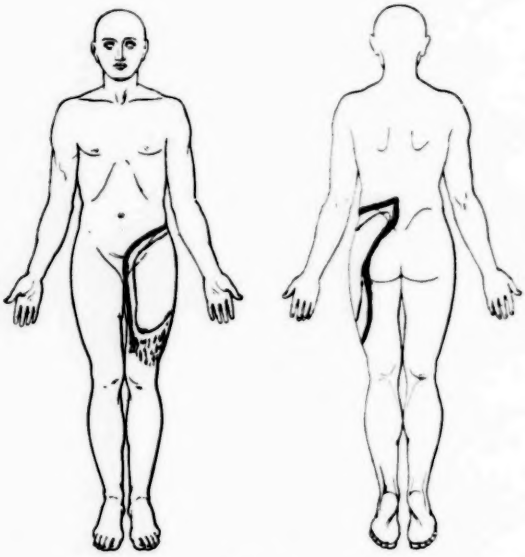

FIG. 1.

child was born in 1907 and is healthy; the fourth was born in 1909. In December, 1909, her husband was admitted to Claybury Asylum, and there, on September 13, 1911, he died; at the autopsy his brain showed the characteristic appearances of "dementia paralytica."

In September, 1910, she began to suffer from pains in the back and down the outer aspect of the left thigh; then the left leg became weak and wasted and her general health again failed.

In July, 1911, she first came under observation. Since this time she has

shown a complete loss of sensibility to painful pressure and the prick of a pin, and to heat and cold, over an area on the front and outer side of the left thigh corresponding to the distribution of the twelfth thoracic and first and second lumbar roots. The anæsthesia to cotton-wool touches was less extensive and the loss less profound (fig. 1). At first the muscles on the front of the left thigh were weak and showed much wasting; there was also paresis and some degree of wasting in the flexor and adductor muscles. The right leg was never affected. The left knee-jerk could not be obtained, and the plantar responses on both sides were flexor.

The patient showed no psychical changes of any kind. Headaches have never been a noteworthy feature and no abnormalities have ever been detected in the territory of the cranial nerves.

On June 25, 1911, the Wassermann reaction was $\frac{\text{serum } 4.4.4.\underline{4.4.}}{\text{cs.f.} \quad 4.4.3.\text{-}.\text{-}.}$

On June 21, 1911, she was injected intravenously with 0·4 grm. of salvarsan, and this dose was repeated on June 27, 1911.

In June, 1912, the wasting of the left leg, though still considerable, was much less extensive than it had been when she first came under observation. The left knee-jerk had returned and, except for the area of profound loss of sensibility observed in 1911, no signs of nervous disease could be detected.

On June 26, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f.} \quad 0.0.0.0.0.}$

On June 27, 1912, she was injected with 0·6 grm. of salvarsan, and on February 6, 1913, and again on August 2, 1913, she was further treated with doses of 0·9 grm. of neosalvarsan.

Since then no new manifestations of any kind have appeared, and in May, 1914, the sensory loss remained exactly as it was when she first came under observation almost three years previously in spite of the fact that both muscular wasting and loss of motor power had disappeared.

More commonly, however, no muscular wasting can be discovered, and sensory signs and symptoms form the only indication that destructive changes are occurring in the nerve-roots and neighbouring structures. If the pains, of which the patient complains, are associated with areas of partial analgesia and thermo-anæsthesia, together with somewhat less extensive loss of sensation to cotton-wool, the diagnosis is not difficult; it is obvious that the posterior roots are affected, especially if the areas of disturbed sensibility have a radicular distribution.

Sometimes, however, no obvious loss of sensation can be found within the area which reacts excessively to pain and other unpleasant stimuli. By extremely careful examination, we could sometimes discover that within these bands of tenderness pricks of a certain strength seemed "duller" to the patient than over the neighbouring normal parts, although they "hurt" more. But in many cases ordinary

clinical methods do not reveal any definite loss of sensation within those areas which react excessively to painful stimuli. They seem, in such cases, to be simply the results of root-irritation uncomplicated by destruction or secondary degeneration (cf. No. 313, p. 30).

Under such circumstances it is almost impossible to differentiate the effects of root-irritation from the tenderness which accompanies referred pain of visceral origin. It is not difficult to distinguish the pain and tenderness due to root-irritation or to visceral disease from that of a pleurisy or local peritonitis; for the latter usually corresponds to the extent of the inflammation and is accompanied by deep, rather than by superficial tenderness. Moreover, the pain of a pleurisy does not radiate round the body from back to front, and if, as is sometimes the case, superficial tenderness is present it lies in front of the point where friction is audible. For any superficial tenderness which accompanies a pleurisy is due to irritation of branches of the intercostal nerves by the pleural inflammation; consequently it will lie in front of the point at which the pleuritic rub is audible and will not extend back to the spine and round the body like the radicular or segmental areas.

But the differential diagnosis between the tenderness due to root-irritation and to referred visceral pain is not uncommonly so difficult that the abdomen has been needlessly opened in many instances.

In the following case (No. 147) the pain and tenderness were so great that a laparotomy was performed although the Argyll-Robertson pupil should have warned the surgeon of the existence of some disease in the central nervous system. Here we could discover no loss of sensation of any kind; the only change consisted in tenderness over the distribution of the eighth and ninth thoracic roots on both sides of the abdomen.

*A Case of Gastric Crises in which the Wassermann Reaction disappeared in the Cerebrospinal Fluid after Treatment with Neosalvarsan, although the Attacks of Vomiting were apparently unaltered.*

*Case* 147.—E. S., male, single, baker; born 1883.

In 1904, at the age of 21, he contracted syphilis and suffered from a "running" followed in turn by a bubo in the right groin, recurrent sore throats and a fall of hair, but no rash. For this he was treated for four weeks only.

In the spring of 1909 after a period of good health he suffered from a severe attack of retching and vomiting. It came on suddenly without any warning and was accompanied by much abdominal pain and tenderness; this first attack lasted four days.

Since this time, at intervals of from four to eight weeks, similar attacks occurred; between them he was perfectly well. They came on without warning and both started and ended suddenly. Of the many drugs tried, morphia only had the slightest effect on the duration of the attacks.

In 1912 laparotomy was performed under the impression that the attacks were due to "gall-stones," but nothing abnormal was discovered in the abdomen.

He first came under observation in May, 1913. At that time he was depressed and his memory was certainly impaired. Speech was unaffected. He had suffered from attacks of apparently causeless vomiting lasting some four to six days accompanied by intense abdominal pain. The attacks whilst he was under our observation were extremely severe. For the last three years at home he had suffered from about one attack in every four weeks, but whilst in Hospital he had four such attacks in seven weeks. In the months preceding admission the severity of the attacks had increased.

He complained of no headache. Vision and the visual fields were unaffected and smell, taste and hearing were normal. The movements of the eyeballs were unbalanced, more especially when looking far outwards to the right and left. The pupils were of pin-point size: in moderate lights the right was larger than the left; neither reacted to light, both reacted on accommodation and convergence. The movements of the face, jaws, palate and tongue were unaffected.

His gait was natural and Romberg's sign was not obtained. The lower extremities were thin, but there was no local wasting of any group of muscles and no hypotonia. Co-ordination of the hands was unaffected.

He complained of spontaneous "rheumatic" pains in the legs; these pains were not associated with any demonstrable changes in the joints. The pain of a prick, heat and cold, two points of the compasses, the situation of a touch, posture, passive movement and the vibrations of the tuning fork were all well recognized on the trunk and extremities. After a gastric crisis tenderness, with hyperalgesia of the eighth and ninth thoracic root-areas, was always present, but three days after each attack these tender areas were no longer demonstrable.

The knee-jerks were obtained on reinforcement and ankle-jerks could be elicited. The plantar responses were sluggish and of the flexor type. The abdominal reflexes and the wrist- and elbow-jerks were unaffected.

At no time had he experienced any difficulty in holding or passing his water or motions.

The movements of the spine were normal.

No abnormal physical signs were found in the heart, lungs, or abdomen. The urine contained neither albumen nor sugar. On the right side of the upper part of the abdomen was a well-healed scar of the laparotomy.

On May 1, 1913, the Wassermann reaction was $\frac{\text{serum } 0.0.0.0.0.}{\text{es.f. } 4.4.1.0.0.}$ and the cells numbered 12 per cubic millimetre.

He was injected on May 5, 1913, with 0·9 grm. of neosalvarsan and on May 10 and again on May 20 with similar doses; after each injection he suffered from a more or less severe gastric crisis.

No "provocative" Wassermann reaction appeared in the serum: on May 15 and again on May 22, 1913, the Wassermann reaction was

serum 0.0.0.0.0.
cs.f. -.-.-.-.-.

The patient's general health greatly improved under the treatment, but it did not affect the frequency or severity of the gastric crises or the signs by which they were accompanied.

On November 25, 1913, he was readmitted for further treatment and, although the manifestations of the disease were unchanged the Wassermann reaction on November 26, 1913, was

serum 0.0.0.0.0.
cs.f. 0.0.0.0.0.

On November 28, 1913, he was treated with 0·9 grm. of neosalvarsan, and again after the injection a gastric crisis developed, lasting on this occasion seven days.

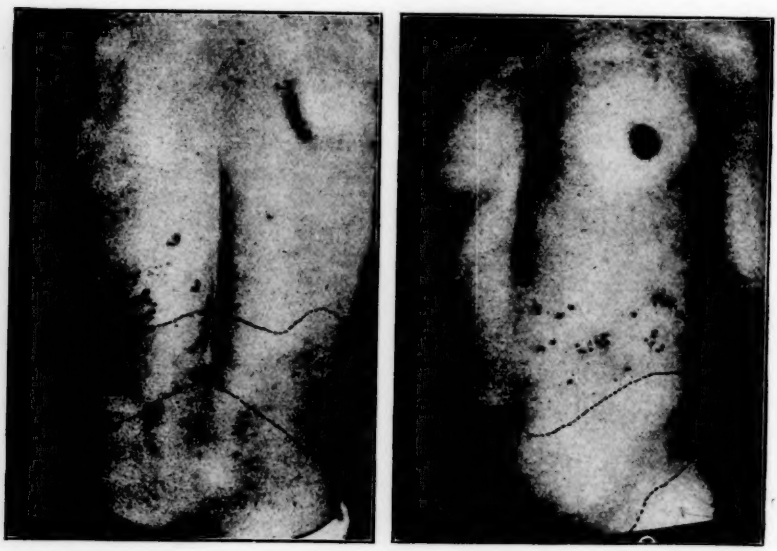

FIG. 2.

Occasionally these root-pains are associated at one time or another in the course of the disease with an outburst of herpes zoster. Thus in No. 125 an attack of zoster appeared over the distribution of the ninth thoracic root on the left side (*vide* fig. 2). This patient had long suffered from a girdle sensation, accompanied by tenderness over

the extent of the tenth and eleventh thoracic areas on both halves of the body. Thus the herpetic eruption on the left side revealed the spread of the meningeal inflammation to the next root above the level of the previous irritative lesions. (For a full account of this case *vide* p. 130.) Similarly in No. 91 the patient had long suffered with pains and excessive reaction to disagreeable stimuli over the distribution of the eighth and ninth thoracic roots on both sides; suddenly he developed pains of a similar character in the left half of the neck, followed by a characteristic herpetic eruption over the second cervical root-area. (For a full account of this case, *vide* p. 73.)

So common are these root lesions in cerebrospinal syphilis, that we look upon them as a most valuable early sign that the structures within the spinal canal have been attacked (cf. No. 313, p. 30). They not infrequently occur in cases where the principal manifestations point to some cerebral lesion, and they are then, as a rule, overlooked. But whatever the other signs and symptoms may be, these areas of pain and tenderness point to affection of the spinal roots and so indirectly to meningeal inflammation; and the occurrence of the changes of the spinal meninges are a significant factor in the interpretation of the results yielded by the Wassermann reaction. Thus these radicular areas of tenderness are of extreme importance, not only in diagnosis and as a guide to early treatment, but also in determining the meaning of the Wassermann reaction in the cerebrospinal fluid.

### § 6.—*Abnormal Reactions of the Pupil.*

Some abnormality in the reaction of the pupils occurs in a large number of cases of syphilis of the central nervous system, apart altogether from tabes dorsalis and dementia paralytica. We have excluded from consideration in this section these two conditions, and also all cases of congenital syphilis; for in-patients who are the subjects of congenital syphilis, changes in the iris, consequent on keratitis punctata and iridocyclitis, frequently make it impossible to test the reactions of the pupils. We were then left with sixty-eight cases of cerebrospinal syphilis; but in five of these patients the iris was fixed to a greater or less extent by adhesions the result of old inflammation, and they were therefore excluded.

Out of sixty-three cases, 33 or 50 per cent. showed some abnormality of reaction in one or both pupils. Of these eleven were totally inactive to light, whilst in the remainder the reaction occurred, but was not

maintained, or the contraction was slight and required an intense light before it was evoked. Occasionally the pupils were badly centred and they were frequently of unequal size; these, however, we have not included amongst the thirty-three abnormal cases, unless they also showed some slowness or other defect of reaction.

If we consider the eleven cases only where the pupils were inactive to light, our experience corresponds fairly well to that of other observers; Uhthoff [22] found ten cases in 100 patients with cerebral syphilis and Nonne ([13], p. 211) states that slighter abnormalities are not uncommon.

We believe that abnormal pupillary reactions are a most valuable sign of infection of the nervous system, especially where the other manifestations are of doubtful significance. In cases of pain and tenderness in the abdomen or chest without signs of visceral disease, or where the symptoms point to neurasthenia the presence of some defect in the reaction of the pupils will clinch the diagnosis in favour of syphilis of the central nervous system (*vide* No. 147, p. 22).

Aortic disease of syphilitic origin is sometimes accompanied by infection of the central nervous system. Thus in one case of this kind (No. 171) the sluggish reaction of unequal excentric pupils was the only sign that the central nervous system was affected.

According to our experience some disturbance of the size, shape or reaction of the pupils to light forms a frequent and an early sign of syphilitic disease of the central nervous system. Abnormal reactions of the pupil are in no way confined to tabes dorsalis and dementia paralytica, but occurred to a greater or less extent in one half of our cases of cerebrospinal syphilis.

### § 7.—*Disturbances of Micturition.*

It is not uncommon, in cases of syphilis of the nervous system, for some disturbance of micturition to be the first cause of the patient's consulting a doctor. But our opportunities of observing this symptom are not so great as with the other conditions described in this section; for a man suffering with some difficulty in micturition will go to a surgeon rather than to a physician. As soon as he is found to be a case of cerebrospinal syphilis, he is treated by the surgeon and does not come under our observation. Our material is not, therefore, a fair sample for determining the frequency with which some defect in micturition forms the initial symptom in cases of cerebrospinal syphilis.

It is, however, well recognized (Nonne ([13], p. 380) that, when syphilis attacks the spinal cord, some difficulty in micturition is usually one of the earliest symptoms. This was so in No. 19, chosen to illustrate this point because the Wassermann reaction in the cerebrospinal fluid rapidly became negative after treatment. Another instance where bladder symptoms appeared as the initial manifestation is No. 125 (see p. 130), a case of combined meningo-vascular and central syphilis.

*A Case of "Meningomyelitis" which started with Bladder Symptoms. The Wassermann Reaction, at first strongly Positive, became and remained Negative in the Cerebrospinal Fluid in consequence of Treatment.*

*Case* 19.—D. B., male, married, grocer; born 1870. In 1890, at the age of 20, this patient contracted a "running," but did not suffer from a sore or any manifestations of secondary syphilis. He was not treated, but remained in good health until 1907; he then developed retention of urine with cystitis and was in bed six weeks.

In February, 1912, after fourteen days of malaise and general pains, he again developed urinary trouble accompanied by pain in the back and abdomen. Whilst he was in bed he developed weakness and stiffness of the right leg. During the month of April, 1912, he seemed to improve, but on May 15, 1912, the left leg became affected and the abdominal pains returned. From that time until his admission on August 1, 1912, he became gradually and progressively worse.

On August 1, 1912, his mental state was unaffected and his speech was natural. He had suffered from no headache, no seizures and no attacks of vomiting. The cranial nerves and fundi were unaffected.

The left hand was unsteady and clumsy in action and the alignment of the fingers was bad. The left leg was completely paralysed and there was grave weakness of the right leg, so that movements could not be performed against slight resistance. The muscles of the lower extremities and of the abdomen, together with the lower portion of the erector spinæ on both sides, showed severe wasting and flaccidity.

He complained of spontaneous pains about the region of the nipples on both sides, and the areas supplied by the third to the sixth thoracic roots were tender to the dragged point of a pin. Below this zone all forms of sensibility were gravely impaired; on the left leg the impairment was greatest to passive movement, posture, the vibrations of a tuning-fork, and the compass-test. On the right leg the loss of sensation was greatest to painful stimuli and to the thermal tests.

Both knee-jerks were much exaggerated, the left more so than the right. Ankle-clonus was readily elicited on both sides, and both plantar reflexes gave an extensor response. The abdominal reflexes could not be obtained.

He could not pass his urine and there was incontinence from overflow, with inability to hold the motions when soft.

On August 2, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.3.2.}$

He was given 0·6 grm. of salvarsan on August 1, 1912, followed by 0·9 grm. of neosalvarsan on August 6, 1912.

On September 2, 1912, he was discharged from hospital able to walk. The wasting of the legs and of the abdominal and erector spinæ muscles after the injections diminished considerably under treatment with massage.

He returned for further treatment on May 19, 1913. At that time the left pupil reacted sluggishly to light whilst the right reacted briskly; otherwise nothing abnormal was discovered in the territory of the cranial nerves. The left leg was smaller in circumference than the right: both legs were spastic and there was obvious ataxy of the left leg on walking. Sensation was impaired on both sides below the level of the umbilicus and the patient still experienced trouble in holding and passing water.

On May 21, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.3.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 4 per cubic millimetre. On the same day he was given another dose of 0·9 grm. of neosalvarsan.

When reinvestigated on February 18, 1914, the nervous condition had not changed from that seen in the previous May, and the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 2 per cubic millimetre.

## Chapter IV.—Syphilis Meningo-vascularis.

This group of syphilitic affections of the central nervous system includes most of the conditions usually spoken of as "subacute," "chronic," "tertiary," and "gummatous." Pathologically they are known to depend, for the most part, on disease of the meninges and vessels. But from clinical evidence alone we can recognize, in many cases, that the signs and symptoms point mainly to affection of meninges and vessels. Thus paralysis and irritation of spinal roots are produced in the majority of cases by meningitis, whilst hemiplegia and the condition usually attributed to "encephalitis" are due largely to vascular occlusion or to the rupture of weakened vessels. We do not require a *post-mortem* examination to recognize that, whatever other lesions may be present, these cases depend for their clinical manifestations on changes in the meninges and vessels.

Now, wherever symptoms and signs point to meningeal and vascular lesions, they are found to be peculiarly amenable to anti-syphilitic remedies. Not only is the disease affected favourably, but the Wassermann reaction, if positive in the cerebrospinal fluid, may become negative within a few months after treatment. At the same time

the excess of cells in the cerebrospinal fluid may become greatly reduced.

But though clinical and serological examination may indicate that any particular case belongs to the meningo-vascular group, we do not believe that a series of patients can be separated into two sharply defined and naturally exclusive classes, those with syphilis meningo-vascularis and those with syphilis centralis. For in most cases there is no essential pathological difference between them; the two conditions are the expression of a similar process acting in two different situations upon different anatomical structures. These anatomical differences lead to a diversity both in the clinical manifestations and therapeutic behaviour. Many cases, as it happens, show no signs of primary destruction other than that in the meninges and vessels; but in some instances the course of the disease and the behaviour of the Wassermann reaction under treatment betray the existence of additional foci of morbid activity deep in the structures of the central nervous system. Such cases are classed by us as "mixed forms," and will be considered in Chapter VI.

In the present chapter we shall deal with those varieties of cerebrospinal syphilis, in which the signs and symptoms, the behaviour of the Wassermann reaction, and the pleocytosis, point to some affection of the meninges and blood-vessels.

Not uncommonly the clinical phenomena of meningo-vascular syphilis are described as "secondary" or "tertiary" manifestations; in some cases a diagnosis of "diffuse gummatosis" is made at the bedside because the first symptoms appeared many years after infection; whilst a similar clinical condition, occurring during the first year, is attributed to secondary syphilis.

We wish to insist on the view that the nature of the clinical manifestations of meningo-vascular syphilis at their first onset does not differ materially according to the period which has elapsed since the disease was acquired. They express the disturbances of structure and function caused by the inflammatory reaction in the central nervous system, and not the stages of syphilitic infection; irritation of posterior roots, cranial nerve paralyses, hemiplegia of vascular origin, will not differ clinically according to the stages of syphilis, but will depend on the extent of the inflammatory reaction and the nature of the structures affected.

Thus the following patient (No. 313) showed signs of profound irritation of many spinal nerve-roots three months after infection,

accompanied by a copious lenticular syphilide, mucous patches, condylomata, and general adenitis. The pyrexia and other signs of secondary syphilis disappeared under treatment with neosalvarsan, and five days after the first injection no abnormal nervous manifestations could be discovered. The cerebrospinal fluid gave a positive reaction, and contained a large excess of polymorphonuclear cells.

*A Case of Secondary Syphilis, within Three Months of Infection, where the signs of Irritation of many Nerve-roots were accompanied by a positive Wassermann Reaction in the Cerebrospinal Fluid and great Pleocytosis.*

*Case* 313.—C. G., female, married; born 1878. This patient was infected with syphilis by her husband early in March, 1914, when six months pregnant with her eighth child. At the date of infection her husband was apparently healthy; subsequently, however, during the months of April and May, he suffered from a series of bad throats, accompanied by malaise, irritability, and pains in the head, trunk, and extremities, but no rash. Towards the end of March, 1914, the patient noticed a more copious vaginal discharge than with any of her other pregnancies, and a few weeks later discovered a sore on her vulva. Early in April she began to suffer from a tired feeling and aching in her lower extremities; then a ham-coloured rash appeared on her abdomen, and subsequently affected almost the whole of the skin of the body. Condylomata appeared around her vulva and anus, followed, about May 17, by the development of a sore throat. After the first week in May she became unable to do her work owing to a severe, dull pain in the head, accompanied by a feeling of sleepiness during the day, with restlessness and inability to sleep by night. Two weeks later she suffered from pains shooting down the inner side of her arms, and down the back of the legs, together with a tight feeling in the lower abdomen and back. About the middle of April, 1914, she sought the advice of her local doctor; the rash was diagnosed as syphilitic and she was treated with mercury by the mouth. In spite of this treatment, however, the rash continued to develop and new manifestations appeared almost daily, until her admission to the London Hospital on June 3, 1914, under the care of Dr. J. H. Sequeira.

On admission, there was a copious lenticular syphilitic rash, widely distributed all over the face, trunk and extremities. The left labium majus was swollen and œdematous. Condylomata were present around the vulva and anus, and there was hyperkeratosis of the soles of both feet. The glands of the groins, at the elbows and on both sides of the neck were enlarged, hard and shotty. She complained of a sore throat, and mucous patches were observed on both tonsils. The temperature was raised and ranged from 98° F. to 101° F. (36·7° C. to 38·4° C.). The rate of the pulse varied from 96 to 120 beats per minute. There was no cardiac enlargement, but the sounds were indistinct and distant. No abnormal signs were detected in the lungs, or in the abdomen, which contained an eight months' pregnant uterus. The urine contained a trace of albumen, but no pus and no sugar.

Mentally she was depressed and worried. She said that for six weeks she had been subject to attacks of crying: she would weep copiously for ten minutes, without any apparent cause, and then stop, "feeling herself again." Mentation was slow, but her memory was little impaired. She felt sleepy, but slept badly and was restless by night. Attention and speech were unaffected. She had suffered from no seizures or attacks of vomiting. Hallucinations and delusions were not present and she had not been troubled by dreams or nightmares.

The special senses were unaffected and the movements of the eyes, pupils, jaws, palate, larynx and tongue were normal. Motion was unaffected, her gait was normal and the grasps of the hands powerful.

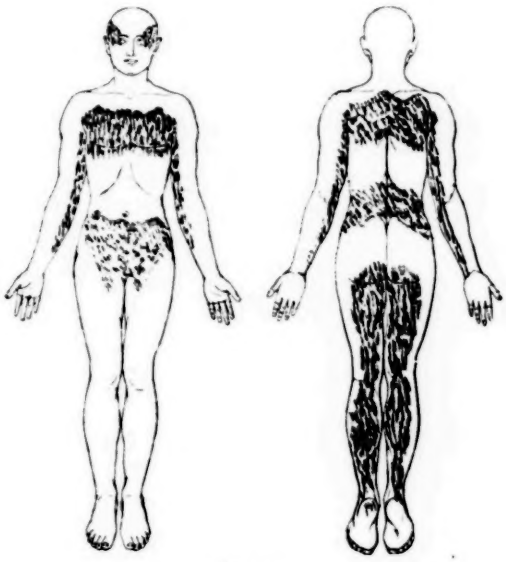

FIG. 3.

She complained of (1) an intense headache with shooting "neuralgic" pains in the temples; (2) of tenderness and shooting pains in the upper part of the chest and along the inner aspect of the axillæ, arms and forearms on both sides: (3) tightness and uncomfortable sensations in the lower part of her abdomen and the upper part of both thighs; (4) shooting, gnawing pains in the backs of the thighs and calves. These pains were aggravated by movement and relieved by rest in bed. Over the areas where the patient complained of pain, the skin was tender and responded excessively to the dragged point of a pin, to pinching and to pressure (fig. 3). She said that these stimuli "felt different," but no sensory loss of any kind could be detected. These

areas corresponded to the peripheral distribution of the second, third, fourth, eleventh, and twelfth thoracic, and the second and third sacral nerve-roots, and to a portion of the distribution of the ophthalmic division of the trigeminal nerves.

With the exception that the right plantar reflex gave an indefinite extension, whilst the left was definitely flexor, all the reflexes were completely unaffected.

She was constipated and had never complained of any difficulty in controlling her motions; but she said that she had found great difficulty in holding and in passing her water, and had at times wetted herself.

The cerebrospinal fluid was collected on June 5, 1914, twenty-four hours after she had been injected with a dose of 0·45 grm. of neosalvarsan, and was tested on June 10, 1914, when the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.0.0.0.}$ On June 5, the cells in this fluid numbered 153 per cubic millimetre; of these cells 75 per cent. were polymorphonuclear, and 3 per cent. plasma cells, and the rest were lymphocytes.

On June 6, 1914, she was further injected with 0·9 grm. of neosalvarsan and this dose was repeated on June 8.

The temperature fell to normal before the second injection was given on the 6th; after this injection she said she felt "much better," the pains ceased and the rash began to disappear. On the 7th the areas of tenderness were no longer definite, and on the 9th they could not be discovered; at the same time the rate of the pulse fell to 72 beats per minute, the patient became cheerful and her mentation improved to a remarkable extent. On June 10, when she was discharged, the rash had almost completely faded, the glandular enlargement was no longer evident, and no abnormal nervous manifestations of any kind could be discovered.

Not only may signs of irritation of spinal nerve-roots make their appearance shortly after infection, but a condition may arise accompanied by signs of gross disease indistinguishable from those frequently seen in the later stages of the disease. Thus, for instance, No. 309, within three months of infection, showed signs of paralysis of many cranial nerves, irritation of the trigeminal, the third, eleventh, and twelfth dorsal, and second and third sacral roots, together with slight difficulty in micturition, a clinical condition exactly comparable to that discovered in No. 3, where the first manifestations of affection of the nervous system did not appear until twenty-three years after infection.

*Widespread Signs of Cerebrospinal Syphilis within Three Months of Infection.*

*Case* 309.—J. W., male, single, stoker; born 1876. In October, 1913, at the age of 37, he contracted syphilis and developed a chancre. On November 4, 1913, he was admitted to the Seamen's Hospital, Greenwich,

with a chancre and a rash which were treated with an intravenous injection of neosalvarsan and black wash. Under treatment the chancre healed and the rash disappeared, and he was discharged feeling well on December 1, 1913.

About three weeks later he began to complain of "pains all over," in the shoulders, knees, wrists, feet and lower abdomen, and intense, throbbing "headaches."

Early in January, 1914, the right side of his face became paralysed, and a few days later he found that he could not walk straight.

On February 10, 1914, he first attended the dermatological clinic of the London Hospital, where he was treated with mercury by the mouth, and on April 5, 1914, he was admitted to Hospital under the care of Dr. J. H. Sequeira.

On admission he was found to be an extremely powerful, well-developed man. He was stone deaf and all communications with him had to be carried on by means of writing. He said that this deafness had come on after an attack of pneumonia at the age of 5, and that in recent times it had not increased. He answered written questions readily and lucidly. He was attentive and gave his history in clear and logical sentences. The drums of both ears showed scars of old perforations. On the prepuce was a scar of an almost completely healed chancre. No rash was present and there was no glandular enlargement. The temperature was not raised; the rate of the pulse was 72 beats per minute.

He complained of severe, grinding and throbbing pains in the head: they were constant and were worst along the base of the skull, in the frontal, temporal and occipital regions. These pains were intensified on pressure. He had not suffered from any seizures or attacks of vomiting and, in spite of the deafness, speech was unaffected. He complained that the sight of the right eye was misty, but the optic discs and fundi appeared healthy. Smell and taste were unaffected. He complained of diplopia and squinted with the right eye. The external rectus muscle on the right side was almost completely paralysed, and all the muscles moving the right eye-ball were paretic. The pupils were well centred, equal and reacted normally to light and accommodation. The muscles moving the right half of the jaw were weak; the masseter on this side contracted feebly and the angle of the jaw swung to the left when the mouth was opened widely. He complained of spontaneous pains along the peripheral distribution of the second division of the right trigeminal and, over an area bounded by the upper margin of the malar bone, the ear, and the lower margin of the mandible, the skin was tender and reacted excessively to the dragged point of a pin. The exact sensory interference over this area could not be determined owing to the deafness of the patient. The upper and lower halves of the face on the right side were almost completely paralysed. The right half of the palate moved badly and the uvula swung to the left on phonation. The sterno-mastoid and trapezius muscles on both sides were well developed. The tongue was protruded straight and was held steadily. All his movements were clumsy and unsteady. The gait was rolling. Romberg's sign was not present.

The grips were powerful. There was no local muscular atrophy and no spasticity.

He complained of spontaneous pains: (1) in the right upper jaw; (2) in the right axilla and in the upper part of the right arm: (3) in the lower abdomen and back on both sides, "a sort of constriction with darting stabs" greater on the left side than on the right; (4) in the back of both thighs and down the calves, more severe and more constant on the left side than on the right. The areas over which the patient complained of spontaneous pains responded excessively to the dragged point of a pin, and corresponded with the peripheral distribution of the second division of the right trigeminal nerve, the right third thoracic nerve-root, the eleventh and twelfth thoracic nerve-roots, and the second and third sacral roots on both sides. Owing to the deafness of the patient a more detailed examination was impossible. The vibrations of a tuning-fork were well recognized everywhere.

The left knee-jerk was greater than the right but both were readily obtained. The ankle-jerks on both sides were brisk. The plantar reflexes were difficult to obtain and were doubtfully extensor in character. The abdominal reflexes were unaffected. The right wrist- and elbow-jerks were exaggerated as compared with those of the left side. At times he had suffered from some hesitation in passing urine, but whilst in bed he had no difficulty in controlling either the rectum or the bladder.

On April 15, 1914, the Wassermann reaction was $\frac{\text{serum}\ 4.-.-.-.-.}{\text{cs.f.}\quad 4.4.4.0.0}$ and the cells numbered 42 per cubic millimetre. He was treated with injections of 0·9 grm. of neosalvarsan on April 6, and on April 8, 1914, followed by eight intramuscular injections of mercury cream. On July 15, 1914, the Wassermann reaction was $\frac{\text{serum}\ 0.0.0.0.0.}{\text{cs.f.}\quad 2.0.0.0.0.}$ and the cells numbered 17 per cubic millimetre.

*Affection of many Cranial Nerves and of the Optic Tract arising Twenty-three Years after Infection. Syphilitic Psychosis. Root Lesions. A strongly Positive Wassermann Reaction in the Cerebrospinal Fluid, which became Negative under Treatment.*

*Case* 3.—A. A., male, married, commercial traveller; born 1864. In 1888, at the age of 24, whilst serving in the Army, this patient caught syphilis: he developed a chancre, which healed under a course of mercury lasting a few weeks only, and was not followed by any rash or sore throat.

From his discharge from the Army in 1892 until 1910 he lived the life of a commercial traveller, taking a considerable amount of alcohol, but on the whole remained in good health.

During the year 1911, he suffered from lassitude and chronic headaches. His memory gradually became bad, and his mental powers decreased. Early in 1912 he had to give up all work, and could not even look after a golf club-house of which he had been appointed caretaker.

He cannot remember what happened to him during the months between March, 1912, and February, 1913; he went from hospital to hospital, but under out-patient treatment gradually grew worse.

In February, 1913, he first experienced diplopia; then for the first time pains became troublesome, and he gradually developed difficulty in holding and passing water.

On April 24, 1913, he was admitted to the London Hospital. At that time he was dull and stupid. He answered questions slowly, but reasonably and correctly. In general conversation his remarks were inconsequent. He gave his history in a rambling manner, and his memory showed enormous blanks when he attempted to recall the events of recent years; it was particularly defective with regard to everyday matters of common knowledge, such as the day on which people usually go to church. He was inattentive, but contented and not over emotional. He slept very heavily, and for the greater part of the twenty-four hours he was drowsy or asleep. He complained of dreadful nightmares and day dreams. He said that he seemed to be always going over his Indian experiences and to be "fighting in odd corners of the globe against fearful odds." "At night, lions and bears seem to be crawling about me," and by day he would misinterpret objects in the wards in terms of his dreams.

Speech was slurred and gabbled, words and syllables being frequently missed out. He had not suffered from seizures, attacks of vomiting or retching.

He complained of severe grinding and gnawing headaches over the vertex and along the base of the skull; the whole scalp was extremely sensitive to pressure.

Both visual fields were much diminished; on the left side the temporal field was almost completely abolished and on the right the nasal half of the field was small, whilst central vision was much impaired. The fields had the same form and outline for all colours. Both optic discs and the vessels of the fundi appeared natural.

Hearing with both ears was unaffected, but taste was much impaired and smell completely abolished.

The right eyelid drooped. The eye movements were unbalanced, and the axes of the eyes rarely moved together; downward movements of the right eye were impaired, and in consequence the patient complained of diplopia (paresis of right third cranial nerve).

The right pupil was dilated, the left small; both were ovoid in outline, and their margins irregular; they reacted extremely sluggishly to light and to accommodation.

The muscles moving the right half of the jaw were paretic and dissociated anæsthesia was present on the right cheek, forehead and anterior portion of the scalp; sensibility to pain, heat and cold was lost over this area whilst that to light touches of cotton-wool was retained. The right cornea was anæsthetic.

The right facial muscles were paretic in movement and at rest showed

overaction. The palate on phonation was drawn to the left, the right half being immobile.

The movements of the larynx were well carried out and swallowing was not affected. On the right side the sternomastoid and trapezius muscles were wasted and there was difficulty in rotating the head.

The tongue was protruded slightly towards the left; fibrillary tremors and wasting were not observed.

The gait was unsteady and clumsy. Romberg's sign was not present. The balance of the fingers was bad and co-ordination of the hands was defective; closure of the eyes did not increase this inco-ordination of the hands. The muscles of the left thigh, more especially those of the extensor group, were wasted. The left buttock was well developed, and the calf muscles appeared natural.

He complained of spontaneous pains in the chest, abdomen and legs, and areas of tenderness, with some loss of sensibility, were present over the distribution of the third and sixth thoracic roots and the third lumbar roots on both sides. Posture and passive movement were well appreciated on the legs and the replies to the tuning-fork tests were accurate everywhere.

The knee-jerks on both sides were exaggerated; ankle-clonus was readily elicited on the right side, but could not be obtained on the left. The abdominal reflexes were absent. Both plantar reflexes gave an extensor response. The right corneal reflex was not obtained, but on the left side it was normal.

The patient complained of difficulty in holding and passing his water, and he not infrequently wetted himself; occasionally also, he was unable to control his motions especially when they were soft.

The spine was straight and moved naturally. No abnormal signs were discovered in the heart, lungs or abdomen and the urine contained neither albumen nor sugar.

On April 30, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.3.2.}$ and the cells numbered 30 per cubic millimetre.

He was given 0·9 grm. of neosalvarsan on May 1, 1913, on May 9, 1913, and on June 26, 1913.

After this treatment on October 29, 1913, the Wassermann reaction became $\frac{\text{serum } 4.4.4.4.1.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 4 per cubic millimetre.

Soon after treatment was begun his mental condition improved enormously: the paresis of the right third, fifth and seventh cranial nerves became less obvious; the wasting of the muscles supplied by the right spinal accessory nerve and that of the left thigh became less noticeable; whilst the spontaneous pains in the limbs and trunk ceased, the areas of tenderness disappeared, and the headache became no longer troublesome. Between April and October, 1913, the patient gained 12 lb. (5½ kg.) in weight.

We have shown that the clinical manifestations of cerebrospinal syphilis do not differ in the various "stages" of infection; in the same

way the pleocytosis and the behaviour of the Wassermann reaction in the cerebrospinal fluid form no guide to the period that has elapsed since the patient was infected. Thus, No. 59, within ten months after infection, yielded a highly positive Wassermann reaction in the cerebrospinal fluid, which rapidly became negative under treatment.

*A Case of so-called "Syphilitic Encephalitis" arising within Seven Months of Infection where a highly Positive Wassermann Reaction both in Serum and Cerebrospinal Fluid became Negative within Six Months of Treatment.*

*Case* 59.—J. G., male, single, railway fireman; born in 1886. This patient contracted syphilis about Christmas time, 1911, aged 25. He developed a sore, for which he attended the Lock Hospital and was circumcized. Shortly after this a rash and sore throat developed. He received injections of mercury whilst an in-patient, and then took mercurial pills regularly from January, 1912, until July, 1912.

In July, 1912, his memory failed and he lost his job "because he was too sleepy and was found asleep on his engine." In the following month, about August 26, he first complained of abdominal pains and general malaise. Fourteen days later he became stuporose and sleepy; for some days he refused to answer questions, speech became affected and then paresis of the left half of the face and of the right hand developed and he passed his water under him. Seven days later he seemed to improve and was able to go about again.

On the morning of October 3, 1912, on waking after a restless night he found that he could not move his legs nor pass his water, and on that day for the first time he passed a motion into the bed.

On October 7, 1912, he was admitted to Hospital under the care of Dr. Robert Hutchison. He complained that he felt "cold," and that his memory was a bit "off," that he felt "tired" and that he did not want to "budge." Cerebration was slow; he repeated orders and sentences addressed to him and eventually attempted to carry them out. Attention was feeble and fleeting. Speech was little affected. When left alone he was drowsy and somnolent and took no interest in the events of the ward. Delusions were not present.

Hearing, smell and taste were unaffected and the optic discs and fundi appeared natural.

The ocular movements were well carried out and ptosis was not present. The pupils were of normal size and reacted well to light and on accommodation. The left side of the face was flattened and appeared paretic on movement; tremor of the lips was observed on both sides. The motor and sensory fifth cranial nerves were unaffected. Movements of the palate, larynx and of deglutition were natural. The tongue showed coarse tremors.

All movements of the upper extremities could be carried out at will in an ineffective, clumsy, unsteady manner. The outstretched hands were held in the posture of weakness with the fingers out of alignment. Both feet were

dropped, the left more noticeably than the right. The muscles of the legs were flabby but not wasted. He was unable to lift his left leg from the bed and could lift the right leg with difficulty only. Rotation of the right hip was relatively powerfully performed and flexion of the right knee was just possible. The lower abdominal muscles were paretic on both sides.

He complained of spontaneous pains in the legs. The calf-muscles were exquisitely tender to pressure, and he resented pressure applied to any of the paretic muscles. Touch, pressure, heat, cold and passive movements were well recognized both from upper and lower extremities. Areas of tenderness showing hyperalgesia to the dragged point of a pin were present on the lower abdomen and back, apparently corresponding with the distribution of the eleventh and twelfth thoracic roots on both sides.

Both knee-jerks were obtained; ankle-clonus was not present and the ankle-jerks were not elicited. The plantar reflex on both sides gave a flexor response. The lower abdominal reflexes could not be obtained, the upper ones were readily elicited. Kernig's test was positive with both legs.

The skin was moist, dirty, oily and had a nauseous odour. The knee-joints on each side contained an excess of fluid.

He was unable to control his sphincters and passed urine and fæces incontinently into the bed. The spine was straight and its movements unaffected.

He was a well-built, well-developed man, weighing 11 st. 10 lbs. (74½ kg.).

The temperature on admission and until treatment was applied was raised to about 100° F. (37·8° C.) and the rate of the pulse varied from 90 to 100 beats per minute.

The vessels were not thickened. There was no cardiac enlargement, but the sounds were shortened and the rhythm tic-tac; no murmurs were present.

He was treated with injections of neosalvarsan, receiving 0·9 grm. intravenously on October 14, October 21, November 4, December 11, 1912, and on March 6, and April 23, 1913.

Under treatment he improved rapidly, and on November 9, 1912, walked out of Hospital. By April, 1913, all the physical signs of gross nervous disease had disappeared, but mentally he was more feeble than formerly and could no longer "think or be trusted." Since this time his condition has remained stationary.

The Wassermann reaction was:—

On October 8, 1912, $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.4.3.}$ On October 30, 1912, $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.1.0.}$ and the cells numbered 16 per cubic millimetre. On December 10, 1912, $\frac{\text{serum } 4.4.4.4.3.}{\text{cs.f. } 4.4.3.0.0.}$ On March 5, 1913, $\frac{\text{serum } 4.4.1.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 4 per cubic millimetre. On April 23, 1913, $\frac{\text{serum } 1.0.0.0.0.}{\text{cs.f. } -.-.-.-.-.}$ On October 29, 1913, $\frac{\text{serum } 2.0.0.0.0.}{\text{cs.f. } -.-.-.-.-.}$ On April, 23, 1914, $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 2 per cubic millimetre.

## [A] Clinical Varieties.

Fortunately no one has attempted to divide the manifestations of cerebrospinal syphilis into separate "diseases," as has happened with "parasyphilis." We speak of syphilitic "encephalitis," "myelitis," "hemiplegia," "muscular atrophy," "combined sclerosis," and give to each case some name illustrative of its principal signs and symptoms. But it is universally recognized that closer observation will usually reveal additional signs of the activity of the virus in some distant part of the central nervous system. One of the most striking characteristics of the activity of meningo-vascular syphilis is the frequency of multiple lesions; in most other diseases of the nervous system we attempt to postulate one lesion to account for all the signs and symptoms, whilst evidence of multiple syphilitic foci is the rule rather than the exception.

Thus hemianopia may be associated with disturbance of the third, fifth, and seventh cranial nerves, and at the same time the sphincters may be affected (No. 3, p. 34). Paralysis of the cranial nerves and optic neuritis may be accompanied by affection of thoracic nerve-roots and of the sphincters (No. 94); in this case a gumma of the scalp betrayed the nature of the lesions in the central nervous system. Cases apparently of pure "myelitis," such as No. 175, may be complicated by abnormal reactions of the pupils. In No. 59 (p. 37) the changes in the nervous system were so widespread, ten months after infection, that the patient showed alteration in speech, affection of the motor and sensory nerve-roots on the trunk, and loss of control over the sphincters.

When a disease assumes such infinite forms it is useless to attempt to separate its manifestations into "types"; each case reveals a distinct combination of signs and symptoms. But for clinical purposes cases may be grouped roughly according to the situation of the principal lesions, and we shall now give some examples of the forms which can be assumed by syphilis meningo-vascularis, indicating at the same time the behaviour of the Wassermann reaction.

### § 1.—*Cerebral Forms.*

Gross cerebral symptoms, consisting of hebetude and more or less severe loss of memory, amounting in some cases to acute dementia, may appear at any time from a few months to twenty years or more after infection. This so-called syphilitic "encephalitis" or "meningo-encephalitis" is universally recognized to depend on inflammatory changes in the membranes, with endarteritis of the vessels of the brain followed by a varying amount of secondary atrophy and sclerosis.

*A Case of Syphilitic Dementia. The Cerebrospinal Fluid gave a negative Wassermann Reaction throughout.*

*Case* 53.—R. F., male, single; born 1880.

He was of good birth, but in 1901 became bankrupt and went to South Africa as a trooper. In 1904 he was in England, in excellent health, but then began to wander again and finally went to Canada. He probably became infected with syphilis about this time. In 1909 and 1910 he worked on a tramp steamer and was admitted to the London Hospital in March, 1912. On admission he lay curled up in bed and never spoke unless he was questioned. He then answered sensibly, but his memory was extremely bad and his attention feeble. He had no conception of time and space and did not know his age or where he was.

He complained of no headache and, as far as his relatives knew, had had no fits or other attacks. He vomited occasionally.

The hands were tremulous, but there was no paralysis, weakness or rigidity anywhere. All movements could be executed well.

No loss of sensation was discovered, as far as he could be tested, and he could recognize the position of his limbs after they had been moved passively.

Knee- and ankle-jerks were brisk; there was no ankle-clonus and both plantar reflexes gave a flexor response.

On ophthalmoscopic examination the vessels of the right disc were seen to be congested and the cup somewhat filled in, but the edges were clear. The left disc was normal.

The pupils reacted well and were equal and regular in outline. There was no ocular paralysis or nystagmus and the movements of the face, tongue and palate were normal.

He gave no indication that he wanted to pass water or evacuate his bowels: thus, unless he was made to micturate at regular intervals, he passed both urine and fæces into the bed. This was, however, due to mental hebetude, and not to true incontinence of urine.

On April 24, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells in cerebrospinal fluid were 2 per cubic millimetre.

In May and June he was treated with mercurial inunctions and on July 7, 1912, he received 0·6 grm. of salvarsan intravenously.

On June 5, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.2.0.}{\text{cs.f. } 0.0.0.0.0.}$

He was readmitted on October 15, 1912, greatly improved. He now talked spontaneously and answered questions readily. He had no recollection of his previous stay in the London Hospital. He read for amusement and wrote well to dictation, many of his old interests had returned and he played golf all day.

His speech was monotonous and face rather expressionless, but otherwise his physical state was unchanged. He had complete control of his sphincters.

On October 16, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.2.0.0.}{\text{cs.f. } 0.0.0.0.0.}$

On October 16, 1912, he was given 0·9 grm. of neosalvarsan intravenously. By October, 1913, he had still further improved. He had reduced his golf handicap to four, and still led an absolutely idle life. On October 29, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.2.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and there was 1 cell per cubic millimetre.

This is a characteristic instance of the effects of syphilis meningo-vascularis in a young man and, although he improved greatly under treatment, he remained, like so many of these patients, without moral energy or a desire to work. Such an after-result is not, however, always entirely due to the disease; most of these young men were inherently untrustworthy in money matters, and disinclined to an orderly life before any signs of nervous disease appeared. To this rule No. 53 was no exception.

Occasionally this form of cerebral syphilis evokes in young men a condition indistinguishable at first sight from dementia præcox. The inhibition of mental processes, want of emotional expression, and negativism, that go to form the characteristic picture of this disease, may be present, but the increased cell-content of the cerebrospinal fluid and the remarkable improvement under anti-syphilitic remedies show that it belongs to the acute syphilitic dementias.

Our second instance is a man, aged 42 (No. 271), in whom acute stupor, followed by dementia, arose twenty years after infection.

*Acute Syphilitic Dementia arising Twenty Years after Infection. Wassermann Reaction Negative in the Cerebrospinal Fluid; Great Pleocytosis.*

*Case* 271.—A. M., male, married, foreman in chemical works; born 1872.

In 1894, at the age of 22, he contracted syphilis and suffered from a sore, for which he was treated for six weeks. No manifestations of secondary syphilis developed, and he remained in good health.

He married for the first time in 1898, and two healthy children of this marriage survive. In 1904 he married for the second time; by this wife he has two living children, and a third died of "weakness and wasting" at the age of three weeks.

In 1909, at the age of 37, his general health failed and he developed leucoplakia of the tongue; since then he has never been well. About Christmas, 1912, he began to suffer from attacks of "rheumatic pains" in the legs. In November, 1913, his memory failed; he became childish in his ways and behaved "like a simpleton." His aptitude for business failed, but he continued at work until January 4, 1914.

On January 14, 1914, he took to his bed. From the 16th until the 19th he lay "unconscious and delirious" with loss of movement in the right

arm, but the leg was never affected. He stayed in bed until the middle of February, 1914. When he got up he could walk well but was weak-minded and feeble and had no initiative.

On March 3, 1914, he was admitted to the London Hospital under the care of Dr. Otto Grünbaum. In the heart, lungs, abdomen and urine no abnormal signs were discovered. The temperature was raised and irregular; it varied from 99° F. (37·3° C.) to 101° F. (38·4° C.); it was usually highest in the evening. There was no tachycardia or increase in the rate of respiration.

He was childish in manner and never spoke unless addressed. He took no interest in his surroundings. He carried out movements on command in a slow irresponsible fashion after a prolonged pause for consideration. Memory was extremely defective. He could not remember any of the details of his illness, nor of the processes employed at the works where he had been foreman. He could not tell the day on which people usually go to church, nor did he know the name of the Prime Minister, though formerly he was a strong party politician. His answers to questions were frequently totally irrelevant, and he had no idea of the relationship between cause and effect. Hallucinations and delusions were not present. There was no grandeur in his ideation; he seemed to be a pure example of severe dementia and for the greater part of the twenty-four hours lay curled up in bed stuporose or asleep.

His speech was slow, phonation monotonous, and articulation defective.

He had suffered from no seizures, but for three days when in bed in January, 1914, he lay in a semi-conscious state and whilst in that condition developed a paresis of the right arm. During the whole of the year 1913 he had complained of attacks of severe headache, but on admission he made no complaint of his head and pressure of the scalp did not obviously cause pain. There was no vomiting during his stay in hospital.

Vision, as far as it could be tested, seemed to be unaffected and the optic discs and vessels appeared healthy. When roused he seemed to hear normally; smell and taste could not be tested.

The ocular muscles were unaffected, but the balance was bad and the patient could not be made to concentrate his gaze on any object for more than a few seconds. The pupils were equal in size, well centred, and reacted normally to light and accommodation. His face was much flattened and quite expressionless. The tongue was intensely unsteady on protrusion. Movements of the jaws, palate and larynx were unaffected.

The patient could hardly stand and his gait was clumsy and unsteady; this unsteadiness was not increased by closing the eyes. The balance of the fingers was bad, and fine movements of the hands could not be performed.

He complained of no spontaneous pains; no gross interference with sensibility was discovered, but the mental state of the patient did not allow of accurate testing.

The skin was oily and inactive; no local vasomotor changes were present.

The knee-jerks and ankle-jerks were brisk but ankle-clonus could not be

obtained. On the left side the plantar reflex gave a flexor response; on the right side either a sluggish extension appeared, or no response was obtained. The abdominal reflexes and the wrist- and elbow-jerks were unaffected.

Unless he were made to pass water at regular intervals he wetted the bed; apparently this was due to his mental state and not to any affection of the sphincter.

The movements of the spine were unaffected.

In the left groin and on the penis were old scars, and the tongue showed the characteristic changes of leucoplakia.

On March 11, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.2.}{\text{cs.f.} \quad 0.0.0.0.0.}$ and the cells numbered 256 per cubic millimetre: the pleocytosis consisted mainly of lymphocytes.

He was injected intravenously with doses of 0·9 grm. of neosalvarsan on March 12, on March 15, and on March 18, 1914. On March 31, 1914, he was discharged from hospital. Under treatment the pyrexia disappeared; he no longer wetted the bed, but his mental condition improved to a small extent only.

Here a pure dementia appeared somewhat rapidly in a man of considerable intelligence twenty years after infection. He might have been mistaken for a case of dementia paralytica without delusions if he had found his way into a workhouse infirmary: but the condition of the cerebrospinal fluid with its enormous excess of cells and negative Wassermann reaction, and also the improvement under injections of neosalvarsan, show that he was a case of the cerebral form of syphilis meningo-vascularis.

This case also illustrates the effect of the secondary cerebral destruction which so often results during the acute stage; arterial blocking and interference with the blood-supply cause secondary necrotic changes which cannot be repaired, and consequently, although the patient's condition improves rapidly, he usually shows some permanent cerebral defect. This man, unlike No 53, was a steady hard-working foreman in chemical works; he was left with a simple residual dementia and not with those defects of will and moral determination so obvious in No. 53 and young men of his group.

Sometimes, however, recovery may be so complete that the patient returns to work and appears to have regained his normal mental and physical health. Thus No. 86 was thought at first to be a case of dementia paralytica in consequence of his mental state, the seizures, affection of speech, and defective reaction of the pupils; this view was rendered more probable by the strength of the positive reaction in the cerebrospinal fluid. The short time, six years, which had elapsed

since infection alone rendered this diagnosis doubtful. However, he improved so greatly under treatment, first with iodides and then with neosalvarsan, that he has returned to full work; at the same time the Wassermann reaction has become negative in the cerebrospinal fluid, and its cell content has sunk from 63 to 2 per cubic millimetre.

*A Case of Cerebral Syphilis simulating Dementia Paralytica. A strongly positive Wassermann Reaction in the Cerebrospinal Fluid became Negative under Treatment. The patient recovered completely.*

*Case* 86.—F. J., married, valet; born 1877.

In 1906, at the age of 29, this patient contracted syphilis; he developed a sore on the penis which was followed by a rash and sore throat lasting over many months and was accompanied by chronic ill-health. He took mercurial pills for two years, between 1906 and 1908.

In 1908 he married. His wife, who is a psychasthenic subject, gives a negative Wassermann reaction in the serum; she has never been pregnant.

Soon after marriage he began to fail mentally, became irritable and forgetful and complained of attacks of severe nocturnal headache. In consequence of this failure he lost his employment and took up work as an insurance agent.

One day, towards the end of June, 1911, five years after infection, whilst riding a bicycle he had a seizure and fell off the machine. He lay on the road for some time but recovered and rode home. In September, 1911, his mental condition became so bad that he could no longer be trusted with money; he became irritable, sleepy and extremely worried. In February, 1912, he was seen by us as an out-patient; whilst attending this department he had another seizure and was in bed for three days. On March 10, 1912, he was admitted to the London Hospital.

On admission he was helpful and obedient in the wards, but was irritable, suspicious, and thought that everyone was talking about him. His attention was fleeting, his remarks inconsequent and he was with difficulty kept to the point. In the ward he rarely talked but spent much time in writing letters to sisters and doctors. These were filled with mistakes in spelling, and he missed out words and syllables; the writing itself was careless, unsteady and tremulous. His memory was extremely defective. Speech was slurred, articulation defective, and syllables were elided.

In June, 1911, he had a seizure, followed in February, 1912, by another severe one; between these dates several minor attacks occurred. He complained of intense headache and a "sense of giddiness all over the head," accompanied by pressure tenderness of the scalp. As an in-patient he vomited several times, usually in the mornings.

Vision was unaffected and the optic discs and fundi appeared natural. Smell and taste were unaffected. Hearing was fair on both sides, otorrhœa from the left ear was observed, and otoscopic examination revealed an old perforation of the drum on this side.

All ocular movements were well carried out. The pupils were equal, centred and reacted sluggishly to light and briskly to accommodation. The face was expressionless. Tremor of the lips was noticeable especially in talking, and the tongue on protrusion showed coarse irregular movements. The palate and larynx were unaffected.

The knee-jerks were exaggerated; the ankle-, elbow- and wrist-jerks were all obtained: the plantar reflexes gave flexor responses. The jaw-jerk was exaggerated.

The sphincters were controlled and the movements of the spine were well carried out.

No gross abnormalities were detected in the heart, lungs, abdomen or urine.

On March 13, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.3.3.0.}{\text{cs.f. } 4.4.4.4.0.}$ and the cells numbered 63 per cubic millimetre.

The case at this time was diagnosed as one of "dementia paralytica," and he was not injected with salvarsan.

As an in-patient he improved slightly. Shortly after his discharge in April, 1912, however, he became unmanageable and was signed up and sent to an Asylum. He remained at the Asylum until February, 1913. As an in-patient there he was treated with iodides, but no mercury; gradually he improved and was discharged as "cured."

On April 12, 1913, he was readmitted to the London Hospital. At this time he was slow in action and in thought. Attention had improved and his memory was better than it had been in 1912, but was still uncertain. He slept heavily and complained of "dreams and nightmares" every night. His writing had improved greatly, was fairly steady and showed no elision of words. Speech was still slow and jerky with some slurring of syllables. Since his discharge from the Asylum he had had no seizures. He still complained of universal headache accompanied by pressure tenderness of the scalp, and was subject to frequent attacks of morning vomiting.

The right fundus oculi appeared healthy; the left, however, showed some swelling of the disc and engorgement of the vessels. Vision was good and the visual fields of normal dimensions. Hearing was fair and there was no otorrhœa.

Ocular movements were well carried out. The right pupil was larger than the left; both were regular in outline and both reacted well to light and to accommodation. The face was not so expressionless as on his previous admission in 1912. There was intense tremulousness of the lips and the tongue was jerky and unsteady in movement.

In carrying out fine movements he was still unsteady and clumsy.

He complained of spontaneous pains shooting along the arms, around the abdomen from the back and in the backs of both thighs and both calves. Areas of tenderness with over-reaction to the dragged point of a pin and other painful stimuli, and considerable sensory impairment, were present over the distribution of the second and the twelfth thoracic, and the third sacral

nerve-roots on both sides. Nowhere was any complete sensory loss found to any form of testing.

The knee-jerks were brisk and equal; the ankle-jerks, wrist-jerks and elbow-jerks were all readily obtained; the plantar responses were flexor. The abdominal reflexes were exaggerated and the jaw-jerk was brisk.

He complained of difficulty in holding his water with precipitancy of micturition, but no true incontinence.

On April 16, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.0.0.0.}$ and the cells numbered 19 per cubic millimetre.

On April 17, April 22, and April 26, 1913, he was injected with 0·9 grm. of neosalvarsan. Under this treatment the spontaneous pains disappeared, his memory improved rapidly, he gained weight and by October 20, 1913, the Wassermann reaction had become $\frac{\text{serum } 4.4.4.4.1.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells had fallen to 2 per cubic millimetre.

On November 1, 1913, he was sufficiently recovered to take up his old employment as valet and confidential servant.

## § 2.—*Hemiplegia.*

Of all the conditions due to meningo-vascular syphilis, hemiplegia is perhaps the best known and the most universally recognized. Many clinicians, however, are satisfied when they have investigated the loss of power in the limbs, tongue and face, and have determined the nature of any disturbance of speech or loss of function of the cranial nerves, which may accompany the hemiplegia.

But as soon as we become interested in the relation of these conditions to the character of the Wassermann reaction, such cases of hemiplegia obviously demand more careful examination. If any order is to be brought into the apparently chaotic results obtained from patients suffering mainly with vascular affections of the brain, we must be certain that there are no signs of disease of the spinal cord or its membranes. We shall, therefore, give two instances of hemiplegia due to meningo-vascular syphilis of the brain, in one of which the clinical signs pointed to diffuse lesions (No. 226), whilst in the other (No. 240) the disease was apparently confined to the cerebrum.

*A Case of Left Hemiplegia with signs of Bilateral Affection of the Pyramidal Tracts and Local Wasting in the left Forearm and Hand. A Positive Wassermann Reaction in the Cerebrospinal Fluid.*

*Case* 226.—G. J., male, married, dockyard policeman; born 1878. He joined the Marines as a youth and served in the Dockyards at Malta and elsewhere, from 1898 until March, 1913. He denied syphilis and gonorrhœa,

but admitted exposure. He married in 1908; his wife has never been pregnant.

From time to time during the whole of the year 1912, he was subject to severe headaches and attacks of shooting pains in his trunk and limbs.

On March 12, 1913, he was suddenly attacked with left hemiplegia for which he was admitted to the Royal Naval Hospital, Malta, where he remained until May 24, 1913. After this attack his speech became affected and his memory failed completely.

He first came under our observation in November, 1913. At that time he was dull, stupid and inattentive. His memory was extremely bad, his speech slow and slurred. He did not complain of headache and his scalp was not tender to pressure or percussion.

Vision, smell, taste and hearing were unaffected and the optic discs and fundi appeared natural.

When looking upwards the ocular balance was defective, but there was no definite paresis of any ocular muscle. The pupils were irregular in outline, oval in shape and unequal, the left much larger than the right; neither showed the slightest reaction to light or accommodation. The left half of the face moved less than the right, whilst movements of the jaws, palate, larynx and tongue were normal.

He walked on a wide base and both legs were stiff and clumsy in movement. Romberg's sign was not obtained. The muscles of the whole left upper extremity, and more especially the flexors of the left wrist, were ill-developed and weak, and the left grasp was feeble. The greatest circumference of the left forearm measured 3·5 cm. less than the right. The left thenar muscles and to a slighter extent the interosseous muscles of the left hand were wasted. There was no wasting of the right upper extremity or of either lower extremity.

Owing to the patient's defective mental state sensation could not be tested accurately, but there was no gross sensory loss.

The skin over the left hand, unlike that of the right, was moist and sodden.

The knee-jerks were exaggerated, but ankle-clonus could not be obtained. The abdominal reflexes were normal and the wrist and elbow-jerks were obtained. Both plantar reflexes gave an extensor response.

At times he wetted the bed, but complained of no difficulty in holding or passing his water.

No abnormal signs were discovered in the heart, lungs, abdomen or urine.

On November 19, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.1.}{\text{c.s.f. } 4.4.3.0.0.}$ and the cells numbered 1 per cubic millimetre.

He was injected with doses of 0·9 grm. of neosalvarsan on November 20, November 27, and December 5, 1913. Before his discharge on December 10, his speech and mental powers had improved remarkably and under treatment with massage the wasting of the left upper extremity had begun to pass away.

*A Case of Hemiplegia where the Disease was apparently confined to the Cerebrum. Negative Wassermann Reaction with Pleocytosis in the Cerebro-spinal Fluid.*

*Case* 240.—E. W., male, single, motor 'bus driver, born 1880. He denied all venereal infection, and there was no scar on the penis, but he admitted exposure on many occasions.

About May, 1913, this patient became subject to attacks of severe headache, pains in his limbs, accompanied by sweating and by mental failure. Early in October, 1913, the pains in his head became worse and he thought that he had caught a "bad cold"; then he developed weakness of the right arm and right leg and lost his taste and smell. On October 15, 1913, he did a complete day's work driving his 'bus for the full journeys, although his right arm and leg felt extremely weak. At the end of the day he collapsed in the garage and was taken home and put to bed. He slept heavily and on the morning of the 16th found that he was unable to move either his right arm or leg, but at that time his speech was not affected. He was brought up to the London Hospital and admitted under the care of Dr. Percy Kidd.

On admission he lay in a half conscious condition with his eyes closed, indifferent to his surroundings; he could be roused by shaking or by shouting, but deeply resented interference. At first speech was little affected, but on the third day after admission he became characteristically dysarthric: there was no dyspraxia. His memory was extremely defective and his attention feeble. He complained of no headache and the scalp was not tender to percussion or pressure. On the first three days after admission he vomited several times.

Smell and taste were abolished, but hearing was not impaired; vision was normal and the optic discs and fundi were unaffected.

All ocular movements could be carried out and there was no ptosis. The pupils were equal in size and reacted normally to light and accommodation. Both upper and lower portions of the right half of the face were paretic. The palate was drawn to the left on phonation and the tongue was protruded to the left. The movements of the larynx and jaws were unaffected.

Neither the right arm or leg could be moved voluntarily. The right upper extremity was flaccid, the right lower extremity somewhat spastic.

Over the right half of the trunk and extremities for the first ten days after admission the patient stated that all sensations felt "different"; but owing to his defective mental state more accurate testing was impossible. No areas of tenderness were discovered and there was no complete sensory loss.

The skin everywhere was oily and had a nauseous odour.

On the right side the knee-jerk was much exaggerated, on the left it was brisk. Ankle-clonus was present on the right side and the plantar reflex gave an extensor response; the left ankle-jerk was readily obtained and the plantar response flexor. On the right side the abdominal reflexes were completely abolished, on the left they were normal.

For five days he suffered from complete retention of urine and had difficulty in controlling his motions.

On October 23, 1913, the Wassermann reaction was $\frac{\text{serum}\ 4.4.4.4.4.}{\text{cs.f.}\ 0.0.0.0.0.}$ and the cells numbered 31 per cubic millimetre.

He was injected on October 18, with 0·6 grm. of neosalvarsan and on October 23, October 30 and November 21, 1913, with doses of 0·9 grm.

On October 23, he developed thrombosis of the right popliteal and femoral veins with œdema of the leg.

On November 12, 1913, the Wassermann reaction was $\frac{\text{serum}\ 4.4.4.4.4.}{\text{cs.f.}\ 0.0.0.0.0.}$ and the cells numbered 20 per cubic millimetre.

Before his discharge on November 30, 1913, his mental state and control over the right leg improved greatly, but the right arm remained completely paralysed. He continued to have difficulty in passing his urine at times. He was able to answer questions lucidly and correctly, but rarely volunteered a remark.

### § 3.—*Affections of the Cranial Nerves.*

Interference with the functions of the third, fourth, fifth, sixth, and seventh cranial nerves on one or both sides and in almost any combination are amongst the commonest manifestations of cerebrospinal syphilis. Innumerable *post-mortem* examinations have been reported showing that these signs are usually produced by endarteritis and meningeal inflammation, and such cases are usually characteristic examples of meningo-vascular syphilis (cf. Nonne [13], p. 192 *et seq.*).

We venture, however, to cite the following cases of this well-known condition because they illustrate the different results which may be obtained with the Wassermann reaction in the cerebrospinal fluid, when meningo-vascular syphilis attacks the cranial nerves and brain-stem. Nowhere are the results of this reaction at first sight more confusing and we shall attempt to show how, in most cases, the explanation of these differences can only be discovered by careful study of the clinical manifestations.

Our first instance (No. 74) is a man, aged 38, who began to suffer from cerebral symptoms seven years after infection. These continued with intermissions for ten years; he then developed an unsteadiness in movements of the eyes, weakness of the right half of the face and palate, together with a bilateral affection of the pyramidal tracts. The Wassermann reaction in the cerebrospinal fluid was at first strongly positive, but became negative in nine months under treatment with neosalvarsan.

The second case (No. 253) was an elderly man, infected twelve years before, who showed all the signs of a complete third nerve paralysis,

associated with pain and loss of sensation over the superior division of the trigeminal nerve. Unfortunately he did not come under our care until he had already received three injections of 0·9 grm. of neo-salvarsan; but in spite of the great improvement in symptoms which followed this treatment he still showed a positive reaction in the cerebrospinal fluid at our first examination, eight months later.

Our next instance (No. 310) is a case of affection of the left crus cerebri, fourteen months after infection, showing the usual signs of paralysis of the third cranial nerve associated with a crossed hemiplegia. The Wassermann reaction was negative in the serum, but weakly positive in the cerebrospinal fluid.

In the next case (No. 128) the signs of complete paralysis of the third nerve were not accompanied by any other evidence of intracranial disease. Here the reaction of the cerebrospinal fluid was at first weakly positive, but became negative within eight weeks of the first injection. The meningo-vascular lesions, revealed by the clinical signs and symptoms, were less widespread than in the previous cases, and consequently the Wassermann reaction was weakly positive in the cerebrospinal fluid.

This leads us on to cases like No. 92, where from the first the Wassermann reaction was negative in the cerebrospinal fluid. This man suffered from paralysis of the left half of the palate, left vocal cord and left sterno-mastoid, which came on suddenly within eighteen months of infection.

One of the most remarkable consequences of syphilitic affection of the brain-stem is polyuria associated with polydipsia; we give an example of this condition (No. 149), where the reaction of the pupils became affected under observation. Here the Wassermann reaction was also negative in the cerebrospinal fluid (cf. Oppenheim [16], p. 53).

Thus in uncomplicated cases of disease of the cranial nerves the behaviour of the Wassermann reaction in the cerebrospinal fluid depends largely on the extent of the intracranial lesions revealed by the signs and symptoms.

But in order that this rule may be true in practice, it is most important to exclude all cases where there is clinical evidence of some concomitant affection of the spinal meninges and roots. This complication of cranial nerve paralyses is commoner than is usually supposed, and failure to appreciate this intraspinal affection will make it impossible to understand the behaviour of the Wassermann reaction in these cases. For a slight disturbance of some cranial nerve may be asso-

ciated with an intensely positive reaction in the cerebrospinal fluid if meningo-vascular changes are also present within the spinal canal.

We have, therefore, added two instances (No. 189 and No. 262) where comparatively trivial affections of the cranial nerves were accompanied by a strongly positive reaction in the cerebrospinal fluid, due to the simultaneous affection of thoracic nerve-roots. Had it not been for careful clinical tests, the true explanation of this reaction in the cerebrospinal fluid would have been missed, and our statistical conclusions would have become chaotic.

*A Case of Affection of several Cranial Nerves on both sides. Strongly Positive Wassermann Reaction in the Cerebrospinal Fluid which became Negative within Nine Months under Treatment.*

*Case* 74.—S. H., male, married, book packer; born 1873. In September, 1895, at the age of 22 he contracted syphilis and developed a chancre, followed by a bubo in the right groin. He was treated for three months and suffered from no secondary manifestations. On his discharge from the Army, in 1902, he married; by him his wife has had (1) a miscarriage in 1903; (2) a miscarriage in 1903; (3) a girl born in 1904; (4) a girl born in 1906, both of whom survived, and are healthy.

In 1902, shortly after marriage, he became subject to attacks of headache, vomiting, and giddiness, called by the patient "bilious attacks." Later, in the same year, he had a seizure accompanied by much headache, some vomiting, and followed by unsteadiness in walking, with numbness of the right leg. After this seizure he attended at the National Hospital, Queen Square, as an out-patient for two years, and was treated with mercury and iodides. He gradually improved, and was in fair health, between 1903 and 1905, except for "bilious attacks."

In 1905 he had another "bad turn," with recurrence of the headache, vomiting, and giddiness, together with a feeling of falling to the right and numbness of the right leg; this attack lasted for about three months.

During the years 1905 to 1912, except for attacks of headache, usually in the frontal region, his health was good, and he was rarely away from business.

In November, 1912, seven weeks before admission to the London Hospital, he went to bed one night feeling fairly well; on the following morning he woke with an intense headache, accompanied by giddiness, retching, and vomiting. On the next day, when he tried to walk, he found that he was unsteady on his legs, and "everything seemed to be going round." After this attack he began to complain of shooting pains and numbness in both legs. He found that either he could not pass urine on desire, or that he was unable to wait long enough to prevent wetting himself.

On admission to Hospital on January 4, 1913, he was found to have thickened and tortuous vessels; the right radial pulse was fuller than the left. The heart was not enlarged, and the cardiac sounds were clear. No

abnormal signs were discovered in the lungs, abdomen, and urine. The temperature was not raised.

His mental state was normal, but he complained of bilateral headache chiefly in the frontal region, and the scalp was tender to pressure and percussion. He had had several attacks of vomiting, the last of which occurred on November 28, 1912.

The fundi appeared healthy, and hearing, smell, and taste were unaffected.

There was a general unsteadiness in ocular movements, which was best observed when the patient turned his eyes laterally; but he complained of no diplopia. The pupils were equal and of moderate size; they reacted well to light and on accommodation. There was no sensory or motor affection of the trigeminal. There was some weakness of the right facial muscles, especially when he attempted to close the right eye. The palate was drawn to the left on phonation, but the vocal cords moved naturally, and there was no difficulty in swallowing. The muscles supplied by the spinal accessory nerve were unaffected. The tongue deviated to the left on protrusion.

He walked uncertainly on a broad base, using his right leg as a prop, and when the eyes were closed fell towards the right. The grasps were powerful, and co-ordination of the hands was carried out fairly well. Dysdiadokokinesia was absent.

He complained of few spontaneous pains, and no loss of sensibility could be discovered.

The knee-jerks on both sides were clonic, the ankle-jerks were extremely brisk, but there was no ankle-clonus. Wrist- and elbow-jerks were readily obtained, and the jaw-jerk was present. The plantar responses on both sides were extensor. The upper and lower abdominal reflexes and the cremasteric reflexes could not be obtained.

The patient complained that he could not hold his urine, nor start the act of micturition at will, but he could control the motions of his bowels.

On January 8, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.3.}{\text{cs.f.} \quad 4.4.4.3.1.}$

On January 14, 1913, he was injected with 0·9 grm. of neosalvarsan, and this dose was repeated on January 22, and again on January 29, 1913. After treatment his general condition improved rapidly, the headache ceased, and he gained weight.

He was again admitted for investigation and treatment on September 25, 1913. He then stated that since the first set of injections he had ceased to suffer from headaches and attacks of vomiting. The ocular movements were still unsteady. The right half of the face was weak. The movements of the palate were now normal, but the tongue still deviated to the left on protrusion. He walked uncertainly on a broad base, and the right leg was stiff and clumsy. The reflexes were exactly as before, and he still had difficulty in holding water and in starting the act of micturition.

On September 24, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.3.0.}{\text{cs.f.} \quad 0.0.0.0.0.}$

*A Case of Third Nerve Paralysis with some Affection of other Cranial Nerves. A Positive Wassermann Reaction in the Cerebrospinal Fluid.*

*Case* 253.—T. G. F., male, married, compositor; born 1857. In 1901, at the age of 44, this patient contracted syphilis; he suffered from a sore on the penis which was diagnosed as syphilitic, but was treated by a chemist for two months only. No manifestations of secondary syphilis followed.

About the beginning of the year 1913 he began to suffer from attacks of severe headache, feelings of tiredness and failing memory. On June 23, 1913, the headache suddenly became worse, a "sort of neuralgia just above the right eye" with "jumping and darting pains." On the morning of June 25 he woke to find that he "saw double." On the 27th he found that the right eyelid had dropped, but "when the lid was opened he saw things as before." From the 23rd to the 30th he was extremely irritable and restless; he said that he had not slept for five nights before his admission on July 1 because of the "horrible pains in the head." On June 30 he completely lost the power of moving the right upper eyelid.

On admission on July 1, 1913, he was mentally clear, but answered questions slowly and with difficulty. His memory was defective for the events of the preceding weeks, but distant memory was unimpaired. He complained that he "kept on seeing strange sights whenever he closed his eyes," and that at home, whilst he was in bed, "the bells seemed to be ringing." At night he was restless and complained of nightmare.

For his work as a compositor he had relied upon his right eye, which he said was "the master"; but to tests he now saw more plainly and distinctly with the left. Both visual fields were of normal extent.

On ophthalmoscopic examination both optic discs and fundi appeared healthy. He was slightly deaf but there was no evidence of internal ear deafness. Smell and taste were unimpaired.

He had suffered neither from seizures nor attacks of vomiting.

He was unable to raise the right upper eyelid. He could move the right eyeball to a small extent outwards and upwards. The muscles supplied by the right third cranial nerve were totally paralysed. The right pupil was ovoid in shape, irregular in outline and larger than the left; it neither reacted to the strongest lights nor to accommodation. Movements of the left eyeball were unaffected. The left pupil was small and reacted naturally to light and accommodation.

He suffered from headache passing from the forehead to the nape of the neck mainly on the right half of the head, which was uniformly tender to pressure. He also complained of pains over the right half of the forehead. Here there was a considerable area of tenderness within which the skin reacted excessively to the point of a pin lightly dragged across it; at the same time the sensation seemed "altered and dulled." Elsewhere over the distribution of the trigeminal, sensibility was unaffected.

On opening the mouth widely the jaw swung over to the right, and on the right side the masseter contracted feebly. The face was expressionless, but

all movements were possible; at rest the right half tended to overact. The movements of the palate and larynx were unaffected. The tongue was protruded straight, but could not be held steadily.

The gait was normal and no change could be detected in motion, sensation, the reflexes, or the action of the sphincters.

On July 8, July 11, and July 18, he was given doses of 0·9 grm. of neosalvarsan. On his discharge on July 22, 1913, although the signs were unchanged he no longer complained of headache or of pain in the right orbital region.

On March 2, 1914, he was readmitted to Hospital. At this time the movements of the right eyeball were considerably more extensive than they had been in the previous July. The lateral movements were well performed but all upward and downward movements were completely lost. The drooping of the right eyelid was less extreme. The right pupil was completely fixed both to light and to accommodation, whilst the left pupil reacted normally. The neuralgic pain and interference with the sensibility of the skin over the right half of the forehead had entirely disappeared, but on the left side a similar tender area was present over the front of the hairy scalp. The skin over this area responded excessively to the dragged point of a pin and to pinching, but was not tender to pressure and over it no loss of sensibility was discovered. The movements of the jaw were well performed and the facial movements were natural. There was no difficulty with swallowing, and the movements of the palate and larynx were unaffected. On protrusion, the tongue deviated to the right and could not be held steadily.

Taste, smell and vision were unaffected. He was slightly deaf, probably owing to wax, as there was no evidence of any affection of the internal ear or nerve-deafness.

Apart from these signs of interference with the cranial nerves no signs were discovered of any gross disease elsewhere in the nervous system.

On March 4, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f.} \quad 4.4.0.0.0.}$ and the cells in the cerebrospinal fluid numbered less than 1 per cubic millimetre.

*A Case of Affection of the Left Crus Cerebri; Right Hemiplegia, with Paralysis of Parts supplied by the left Third Cranial Nerve. Negative Wassermann Reaction in the Serum, Positive Reaction in the Cerebrospinal Fluid.*

*Case* 310.—G. W., male, married, aged 36, butcher; born in 1878. In January, 1913, this patient contracted syphilis. He developed a hard chancre, followed by general malaise, ulceration of the throat which lasted for three or four months, and a generalized syphilitic rash. He was treated with mercury by the mouth for nine months.

About November, 1913, his mental condition failed and he became subject to severe attacks of headache. On December 24, 1913, he was seized with pains in the back and an extremely severe headache, which in the course

of the day was followed by tremor and some difficulty in moving the right arm and leg; before evening the right arm shook so badly that he could not hold small objects in his hand. He was treated for "neurasthenia" and gradually improved. On February 14, 1914, he went for a holiday to the seaside and whilst away, on February 27, the left eyelid dropped and the right side of the face became paralysed. He was put to bed and shortly afterwards developed the stuporose condition in which he was admitted to the London Hospital on March 14, 1914, under the care of Dr. Theodore Thompson.

The patient was a well-developed, muscular man. His skin was oily and had a nauseous odour. His temperature before treatment oscillated between 97·5° F. (36·4° C.) and 99·8° F. (37·7° C.) The rate of the pulse was not increased, but the cardiac sounds were muffled and indistinct. No abnormal signs were discovered in the lungs or abdomen and the urine contained neither albumen nor sugar.

He was somnolent and stuporose, but could be roused by shouting and then answered questions in an illogical, inconsequent manner. Frequently he repeated words and sentences several times before he attempted to respond, and then gave an answer which was irrelevant or made a movement which had little or no relation to the command given. He rarely spoke spontaneously. He lay in bed sleepily with his eyes closed for the greater portion of the twenty-four hours, but at times he roused himself and became restless and difficult to manage. His voice was monotonous and many syllables and words were slurred. He yawned frequently. Delusions and hallucinations were not present. He complained of no headache and seemed happy and contented. He did not suffer from fits or attacks of vomiting.

He complained of diplopia and mistiness of vision; on ophthalmoscopic examination the optic discs and fundi on both sides appeared healthy. He responded extremely slowly to all auditory stimuli, but there was no deafness due to disease either of the internal or middle ear. Smell and taste were unaffected.

The movements of the right eyelids and eyeball were natural. The right pupil was well centred, of average size and reacted normally to light and on convergence. The left upper lid was dropped. The movements upwards and inwards of the left eyeball were extremely defective. The left pupil was dilated; it neither reacted to strong lights nor on attempts at convergence. The movements of the palate, larynx and jaws were unaffected. The tongue could not be held steadily and on protrusion it deviated to the left. He complained of difficulty in swallowing and often had to be fed with a nasal tube. The movements of the sterno-mastoids and trapezii were normal.

He could not stand and all movements of the arms and legs were clumsily performed and paretic. The right grip was feeble, the left fairly strong. The alignment of the fingers and wrist on the right side was bad and they could not be held steadily. The power of both legs was much impaired, the right to a greater degree than the left. At times he was restless and waved his limbs about in an inco-ordinate manner.

He complained of no spontaneous pains and no sensory loss could be discovered. The vibrations of the tuning-fork and the shape, size, and form of objects placed in the hands were well recognized.

The right knee-jerk was greatly exaggerated, the left was present. Ankle-clonus was readily elicited on the right side, but could not be obtained on the left. On the right side the plantar reflex gave an extensor, on the left a flexor response. The wrist- and elbow-jerks on the right side were exaggerated. The right abdominal reflexes were almost completely abolished.

On admission he passed urine and fæces incontinently into the bed.

On March 18, 1914, the Wassermann reaction was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 4.1.0.0.0.}$ and the cells numbered 39 per cubic millimetre.

He was injected with 0·3 grm. of neosalvarsan on March 18, 0·6 grm. on March 20, and 0·9 grm. on March 23, March 25 and March 27, 1914: he also received intramuscular injections of 0·002 grm. of hydrargyri perchloridi three times daily between March 20 and April 9, and 2 grm. of potassium iodide three times daily by the mouth.

Under this treatment the signs of a lesion within the brain-stem persisted unchanged, but the mental condition brightened and he became more rational and less drowsy.

The Wassermann reaction on May 13, 1914, was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 13 per cubic millimetre.

*Paralysis of the Third Cranial Nerve with a Positive Wassermann Reaction in the Cerebrospinal Fluid, which became Negative within eight weeks.*

*Case* 128.—F. R., male, married, labourer; born 1866. In 1884, at the age of 18, this patient contracted a "running." He had no recollection of any sore, or any manifestation of secondary syphilis. He married for the first time in 1885: of this marriage there were no children, and this wife died of chronic pulmonary tuberculosis at the age of 28. He married his second wife in 1893; by her he had two children, the one born in 1894 and the second born in 1903.

Until the beginning of the year 1913 his health was fairly good, but on February 15, 1913, he noticed that his left eyelid had dropped. During the next seven days complete paralysis of the left third cranial nerve developed which began with troublesome double vision lasting two days.

On admission on February 22, 1913, there was complete paralysis of the left third cranial nerve with ptosis, diplopia on looking upwards and downwards, and a large fixed pupil. The external rectus and superior oblique muscles on this side acted perfectly and the movements of the right eyeball and pupil were unaffected. Vision and visual fields on both sides were normal and both fundi and discs appeared healthy. No further physical signs of nervous or other disease were discovered. A scar was seen on the penis and the shins showed typical tissue-paper scars.

On March 5, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.1.0.0.0.}$ and the cells numbered 11 per cubic millimetre.

He was injected with 0·9 grm. of neosalvarsan on February 25, 1913, and this dose was repeated on March 8.

On April 23, 1913, the physical signs were unchanged, but the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered 11 per cubic millimetre.

In May, 1914, he still showed an almost complete paralysis of the left third cranial nerve, but in the twelve months since he was first treated no new manifestations had appeared.

*A Case of Paralysis of the Palate, the Vocal Cord, the Trapezius and Sterno-mastoid on the left side. Root Lesions of the Left Upper Cervical Nerves. Medullary "Fits" and Glycosuria following Injections of Neosalvarsan.*

*Case* 92.—H. K., male, single, hairdresser; born 1892. In the autumn of 1911, at the age of 19, the patient caught syphilis. He developed a chancre, but no rash or other secondary manifestations followed. He attended twice at the Lock Hospital: at the end of this time the chancre had completely healed.

His health then remained fairly good until October, 1912, when he began to complain of left-sided headache "in the temples" and earache on the left side. He attended the London Hospital for some weeks under the care of Dr. Lambert Lack.

On January 13, 1913, after a period during which he complained of "buzzings in the left ear," he suddenly lost his voice and became unable to swallow. "My throat became as if it should have been sore but was not." Then he became subject to pains shooting down the left side of the neck to the point of the left shoulder, and became "depressed."

On February 25, 1913, he was admitted to the London Hospital. On admission he complained of severe pains in the left side of the neck, difficulty in swallowing, an alteration in his voice, intense thirst, mental depression, and left-sided temporo-occipital headache with severe pain over the left external auditory meatus.

He was very emotional, but attention and memory were good and he slept well.

Ocular movements were well carried out and he had never complained of double vision. The pupils were well centred and reacted naturally to light and accommodation. The face acted normally on emotion and on voluntary movement. Movements of the jaws were well performed, and there was no alteration in the sensibility of the skin supplied by the fifth cranial nerve.

On phonation the palate was drawn up to the right, owing to complete paralysis of the left half. At times he had difficulty in swallowing solids; he never experienced any difficulty in swallowing fluids, and the difficulty with solids varied much from time to time. He showed no tachycardia and no

alteration in the respiratory rhythm. The left vocal cord lay in the "cadaveric" position and was immobile on phonation. The left shoulder was dropped and the sternomastoid and trapezius muscles on this side were paretic and wasted, more especially their upper halves. The levator anguli scapulæ and other muscles of the shoulder region were unaffected. The tongue showed no wasting or fibrillary twitchings, and was protruded straight.

Vision and the optic discs on both sides were unaffected.

He complained of noises and "buzzings" in the left ear, but no definite loss of hearing could be determined on examination. Smell and taste were unaffected.

The limbs were fairly well developed and no local wasting of muscles was present. The hands were steady and the fingers well aligned. The grips and gait were natural.

He complained of pains in the left side of the neck and over the distribution of the second, third and fourth cervical roots, on the left side tenderness was present to the dragged point of a pin and to pinching the skin. The back of the pharynx and the fauces were totally insensitive to a brush.

All the reflexes were normal. The knee-jerks were readily obtained and both plantar reflexes gave a flexor response. The sphincters were unaffected.

The heart, lungs and abdomen showed no abnormal physical signs, and on admission the urine contained neither albumen nor sugar. A scar was visible on the penis and another was seen due to old and recent inflammation on the front of the right shin. The bone under the scar on the right shin was thickened (gummatous periostitis).

On March 7, 1913, the Wassermann reaction was $\begin{matrix}\text{serum } 4.4.4.4.0.\\ \text{cs.f.} \quad 0.0.0.0.0.\end{matrix}$

On March 7, March 12, and again on March 18, 1913, he was injected intravenously with 0·9 grm. of neosalvarsan.

On March 16, 1913, the patient had seven "medullary fits," in which he became cyanosed, developed bradycardia, became drowsy and the temperature rose to 100° F. (37·8° C.). After these attacks glucose and aceto-acetic acid appeared in the urine. On March 17, 1913, the urine contained 0·7 per cent. glucose and gave a definite Gerhardt and Rothera reaction for aceto-acetic acid. The glycosuria persisted for forty-eight hours after the onset of these attacks.

On April 15, 1913, the physical signs remained unchanged, except that the movements of the palate were now symmetrical and there was no glycosuria. The patient no longer complained either of headache or of noises in the ears.

*A Case of Polydipsia with Polyuria and Recurrent Attacks of Pyrexia due to Syphilis. Subsequent Development of Defective Pupillary Reactions.*

*Case* 149.—B. S., male, single, labourer; born 1885. In 1906, at the age of 21, he contracted a chancre, for which he was treated for six weeks; no secondary manifestations followed, and he remained in perfect health.

In July, 1912, six weeks before his first admission to the London Hospital,

under the care of Dr. Percy Kidd, he began to suffer from a severe dull headache, which was worse towards evening and when he was lying down. Two weeks afterwards he took to his bed with a febrile illness diagnosed as "typhoid fever"; the fever lasted until admission to hospital four weeks later and was accompanied by intense thirst and polyuria.

On admission, on August 20, 1912, he was a well-covered healthy man, complaining of severe headache and great thirst. He was somnolent, introspective and inattentive. His scalp was everywhere exquisitely tender to pressure. The cranial nerves, motion, sensation, the reflexes and the special senses were unaffected.

His temperature was 102° F. (39° C.), the rate of the pulse 120 per minute, and the rate of respirations 24 per minute. The quantity of urine passed in twenty-four hours varied from 5,700 to 9,000 c.c., but albumen and sugar were not present.

On August 28, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.2.}{\text{cs.f. } 0.0.0.0.0.}$

On August 24, after three days strict confinement to bed, the temperature fell to normal.

On August 30, 1912, he received 0·9 grm. of neosalvarsan intravenously and similar doses on September 3 and 9. Under treatment the headache had disappeared, but the polydipsia and polyuria persisted for some weeks unchanged.

On October 12, 1912, his headache reappeared in a different form. After some trouble at home he had a seizure in which he "seemed to come over giddy"; his head was "bad behind the eyes" and he again became irritable and introspective, complaining of pains all over the body.

On November 11, 1912, he was readmitted; at that time he was dull and somnolent and altered mentally. The right pupil was now widely dilated, whilst the left was of normal size; both reacted sluggishly to light and immediately dilated again; the reaction to accommodation was normal. The tongue could not be held steadily. Otherwise no abnormal signs were discovered in the nervous system. The quantity of urine passed on this occasion was still high and on an average 3,000 c.c. in twenty-four hours. On November 12, 1912, the Wassermann reaction was $\frac{\text{serum } 4.3.2.1.0.}{\text{cs.f. } 0.0.0.0.0.}$

He was readmitted on January 4, 1913, complaining of "general pains and muzziness of the head," but there was no polyuria and the daily quantity of urine passed was, on an average, 1,200 c.c. On February 5, 1913, the Wassermann reaction was $\frac{\text{serum } 3.3.3.2.1.}{\text{cs.f. } 0.0.0.0.0.}$

Since this time he has been continuously under observation and has had three distinct pyrexial attacks followed by intense polyuria similar to that observed when he was first admitted in August, 1912.

On November 4, 1912, January 22, 1913, and on September 23, 1913, he was given injections of 0·9 grm. of neosalvarsan.

On September 24, 1913, the Wassermann reaction was $\frac{\text{serum } 2.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$

*Affection of many Cranial Nerves, together with several Spinal Roots. Positive Wassermann Reaction in the Cerebrospinal Fluid.*

*Case* 189.—A. O., male, married, electrician; born 1858. This patient joined the Army in 1875, transferred himself to the Marines in 1877, and then travelled round the world "having a good time" from 1885 to 1886.

He denied syphilitic infection, but admitted frequent exposure, and in 1883 he suffered from an illness called "malaria," with a rash, fever, and aching all over. He married in 1886 and his wife had five children born between 1887 and 1894, all of whom survive and are healthy.

In March, 1912, he began to suffer from "sciatica," shooting pains in the back and inner side of the right thigh. These pains were severe for four or five months, and towards the end of the attack were accompanied by a feeling of tightness and shooting pains in the lower abdomen. He was admitted to the General Hospital, Detroit, in June, 1912, and remained there until December, 1912. Under treatment with rest and morphia the pains became easier.

In October, 1912, a lump appeared at the angle of the right lower jaw; this was excised on March 6, 1913, and proved on microscopical examination to consist of gummatous material. Towards the end of March, 1913, the right half of his face and the right eye became "dead and numb." Then the right eye seemed to become "stiff and dry" and ceased to secrete tears, and he completely lost smell and taste. He wasted rapidly, and between January, 1912, and June, 1913, his weight fell from 11st. 2 lb. to 8 st. 9 lb. (from 71 to 55 kilos).

On April 5, 1913, he left the United States feeling "tired and good for nothing." On the voyage home he developed a squint and later diplopia; at the same time he began to suffer from severe pains in the head and found difficulty in moving his jaws and tongue.

He was seen by one of us on June 17, 1913, and admitted to the London Hospital under the care of Dr. Percy Kidd. On admission he was a wasted, worn man. His memory and attention were good and speech was unaffected. He had not suffered from seizures or attacks of vomiting. He complained of headache passing from the frontal region through the temples into the back of the neck, worse on the right side than on the left, and the scalp over these regions was tender to pressure.

Smell was completely abolished and taste was almost lost. He said that objects appeared hazy and misty, but though the vessels of the fundi were engorged and pinker than normal, the optic discs appeared healthy. On both sides hearing was impaired and he could hear a watch at the distance of 3 cm. only, which could be heard well by a normal person at 40 cm. On the right side bone-conduction was more defective than on the left.

He suffered from a permanent right-sided squint and complained of diplopia. The right external rectus muscle was completely paralysed, the left acted normally. The muscles supplied by the 3rd and 4th cranial nerves on both sides

acted powerfully. The pupils were well centred and reacted briskly to light and accommodation, but to light the reaction was ill-sustained and was accompanied by hippus.

He complained that his artificial teeth could no longer be made to fit; on opening his mouth widely the jaw swung over to the left and the right masseter and temporal muscles on volition contracted feebly. He complained of shooting neuralgic pains and numbness over the whole of the skin supplied by the right trigeminal nerve. Over this area there was gross sensory loss of sensibility to the prick of a pin, to the hot and cold tubes, and to the light touch of cotton-wool.

The palpebral fissures were equal and the movements of the frontalis symmetrical, but there was much weakness of the lower portion of the right half of the face.

On phonation the uvula was drawn up to the left; the tongue was protruded towards the right, although the left half was also weak; he said that the tongue felt too big for his mouth and would not "do its work."

Swallowing was unaffected and the movements of the larynx were normal.

The trapezii and sternomastoid muscles were well developed. There was no polydipsia or polyuria.

The gait was somewhat rolling and unsteady, but Romberg's sign was not present. The grasp of the left hand was feeble and in movement this hand was clumsy. A definite static tremor of the left upper extremity appeared when the hands were stretched out in front of the trunk. The patient experienced no difficulty in rapidly rotating the wrists. The lower abdominal muscles, more especially on the right side, were paretic, and the patient's abdominal wall bulged when he raised his head from the bed. The muscles on the inner side and along the back of the right thigh were somewhat wasted.

The patient complained of (i) spontaneous neuralgic pains in the right side of the face; (ii) of tightness in the right half of the abdomen and back above and below the level of the umbilicus; (iii) shooting pains in the front of the thigh and over the lower part of the abdomen on the right side; (iv) of shooting pains over the back of the right thigh and calf. The skin in these regions on the trunk and lower extremity was tender and reacted excessively to the dragged point of a pin. At the same time there was some sensory loss over those areas to the prick of a pin. The areas corresponded to the peripheral distribution of the 9th, 10th and 12th thoracic, the 1st lumbar and the 2nd and 3rd sacral nerve-roots on the right side.

The knee-jerks were exaggerated, the left brisker than the right; both ankle-jerks were readily obtained, but ankle-clonus was not present. On the right side the plantar reflex gave a flexor, on the left an extensor response. The wrist- and elbow-jerks on the left side were brisker than on the right. Abdominal reflexes could not be obtained.

Previous to his admission he had experienced difficulty in holding his water, but whilst under observation this was no longer present.

No abnormal physical signs were discovered in the heart, lungs or abdomen, and the urine contained neither albumen nor sugar.

On June 25, 1913, the Wassermann reaction was $\frac{\text{serum}\ 4.4.-.-.-.}{\text{cs.f.}\ 4.4.4.0.0.}$ and the cells numbered 70 cubic millimetres.

He was injected on June 27, July 5, and July 10, 1913, with 0·9 grm. of neosalvarsan. Before his return to America in October, 1913, he had improved greatly. All spontaneous pains had ceased, he walked well and no longer complained of the difficulty with his mouth and jaws.

*Affection of the Trigeminal, Auditory, Vestibular, and Glossopharyngeal Nerves, together with some Spinal Nerve-roots. Strongly Positive Wassermann Reaction in the Cerebrospinal Fluid which became Negative under Treatment.*

*Case* 262.—H. O., male, married, cabinet maker; born 1884. In 1903, at the age of 19, he contracted syphilis and suffered from a hard chancre which was not followed by any manifestations of secondary syphilis; the sore healed in a few weeks without treatment.

In 1905 he was admitted as an in-patient into the Seamen's Hospital, Greenwich, where he remained six months, complaining of pains in many joints and in the heels and back of the calves.

He married in 1907; of this marriage a healthy child was born in 1908, in whose serum the Wassermann reaction was negative; his wife had had no miscarriages.

In 1909 he suffered from a rash on the back of both forearms, lasting a few weeks only, and about the same time a gumma developed on the left shin which healed under the administration of iodides.

Between 1909 and the summer of 1912 his health was good, but in the autumn of 1912 he began to complain of pains in the head, passing from the lower part of the forehead along the temples into the back of the neck: he described the pains as "gnawing and continuous, like the rheumatics." The pains at first came on in attacks only; in 1912 he suffered from an attack about once a week, but later they became more frequent, lasted longer and "left his head sore." About June, 1913, his scalp became so tender that "he could no longer wear a hat." He said that the pains were always worse when he was in bed at night, and when he was at work; they were especially aggravated by the noise of the machinery; at times when the pains were severe he felt sick, but he had never actually vomited.

About May, 1913, he became drowsy by day, but began to sleep extremely badly. Then he became subject to "dreadful nightmares"; he would wake up in "frights" thinking that a "circular saw was cutting off his fingers and the like."

He continued at work until the middle of October, 1913. One evening in that month, whilst playing ludo with his wife, he seemed to "come over giddy" and fell off his chair. He was helped to bed, where he remained in a half-conscious condition for three days: he was away from work at this time for three weeks. Then, after working for nine days, he had a second attack of giddiness in the workshop. He felt "as if falling backwards and to

the left," sat down, became dazed but did not actually fall or lose consciousness. After this attack until the time of his admission to the Hospital he did no work. Between the middle of November, 1913, and February, 1914, he had five distinct "giddy" attacks, and on three separate occasions actually fell in the street. Between them, whenever he closed his eyes he had a feeling "as if he were falling backwards and to the left." This feeling of falling was intensified by lying on his left side. During the attacks the whole world seemed to become misty and fade away, and "things seemed to move away to the left to a buzzing noise in the left ear"; apart from the attacks he had never heard this noise in his ear. In the attacks he never actually lost consciousness, but on one occasion he voided urine. After the attacks he usually found that a tender spot had appeared below and behind the auditory meatus on the left side. Between the attacks he was drowsy and dazed, and so unsteady on his legs that he was unable to stand without support.

About October, 1913, he began to suffer from a series of shooting "rheumatic" pains in the right arm, forearm, and ulnar fingers. From that time he had also experienced a "tight, funny sensation" in his abdomen at about the level of the umbilicus, passing round the sides into the back at a slightly higher level.

He also volunteered the statement that since the illness began he had gradually lost his memory, become less able to concentrate his thoughts, was no longer able to look after money matters, and "had lost all his knack with his fingers."

He was admitted to the London Hospital, under the care of Dr. Robert Hutchison, on February 13, 1914.

On the penis was the scar of a chancre; gummatous scars were present on the left shin and a raised tender swelling, evidently a gumma of the peritoneum, was present on his right shin. A peculiar herpetiform rash occupied the skin of the nose, whilst both forearms were covered with a raised, scaly itching, circinate eruption, which had been present for eighteen months.

He was irritable, passionate and excitable. He acknowledged that he was less capable in business than he had been formerly and that as a handicraftsman he had lost all his habitual skill. His memory for recent events was defective, but fair for past events. His attention was impaired. He spelt badly and was restless at nights. His speech was natural. Under observation he suffered from no fits or attacks of giddiness, nor did he vomit. He complained of a constant, intense headache which was increased by noise or sitting in front of the fire. The whole of his scalp was exquisitely tender to pressure.

Vision, smell and taste were unaffected, but the vessels of the fundi were engorged and tortuous; there was, however, no swelling of the disc or œdema of the fundus. Hearing on the left side was impaired, and tests showed that this was due to an affection of the internal ear or auditory nerve; on the right side hearing was unaffected.

Irregular movements of the eyeballs appeared on extreme lateral movement, but there was no true nystagmus. The eyes were prominent, but there was no paresis of any ocular muscle and diplopia was absent. The pupils reacted slowly to light with the appearance of rhythmic contractions and dilatations; they were equal in size, well centred and reacted normally on convergence and accommodation. The facial movements were unaffected and the muscles of the left half showed less tone than those of the right. The movements of the jaw were natural. He complained of spontaneous pains of a "neuralgic" character in the left side of the face above the malar bone passing back to the line of the scalp and as far forward as the middle line of the forehead. Over this area the skin was tender and showed over-reaction to the dragged point of a pin together with some diminution, but no complete loss of sensibility to pin-prick, heat or cold; no change could be discovered on testing with cotton-wool. On phonation the uvula was drawn up to the right but the tongue was protruded straight and held steadily, and the movements of the larynx were unaffected. The trapezii and sternomastoids were well developed and swallowing was unaffected.

His gait was rolling and ataxic; he tended to fall to the left when his eyes were open and could not stand when his eyes were closed. When he was made to walk round a chair he fell inwards when walking counter-clockwise and outwards when walking clockwise. When he crawled the left shoulder drooped and he tended to roll over towards the left. The tone of the muscles of the left upper extremity was less than of the right. He experienced great difficulty in rapidly rotating his left hand, and this hand was clumsy in performing co-ordinated movements. There was no hypotonia of the legs and no local muscular wasting.

He complained of spontaneous pains (i) in the left side of the face; (ii) in the right axilla and along the inner border of the arm and to a less extent of the forearm, which he called the "rheumatics of the arms"; similar pains occasionally also appeared on the left side, but these were less constant and less severe; (iii) tight feelings and shooting pains in the abdomen at the level of the umbilicus, passing round to the back at a somewhat higher level; (iv) shooting pains at the back of the right and left thighs below the buttocks and in the back of the calves ("rheumatics in the legs"). To the dragged point of a pin and to pinching of the skin areas of tenderness were discovered, corresponding with the peripheral distribution of the ophthalmic division of the left trigeminal nerve, of the 2nd, 3rd, and 10th thoracic, and of the 2nd and 3rd sacral nerve-roots on both sides. The tender area supplied by the 10th thoracic nerve-roots showed a considerable loss of sensibility to the prick of a pin and to the hot and cold tubes. The vibrations of a tuning-fork and passive movement and posture were well recognized everywhere.

The knee-jerks were obtained and equal, the ankle-jerks were normal. On the left side the plantar reflex gave a flexor, on the right an extensor response. The abdominal reflexes and the wrist- and elbow-jerks were natural.

He experienced no difficulty in holding or passing water.

No abnormal physical signs were discovered in the heart, lungs, abdomen or urine.

On February 19, 1914, the Wassermann reaction was serum 4.4.4.4.4. c.s.f. 4.4.4.4.0. and the cells numbered 55 per cubic millimetre.

He was injected on February 18, February 21, and March 2, 1914, with doses of 0·9 grm. of neosalvarsan.

After treatment he improved slowly and gradually. The headaches ceased, his memory and aptitude returned, he began to sleep normally and was no longer troubled with dreams or restless nights. He returned to work on April 6, 1914; he was then able to carry out his work up to his old standard and earn full wages. On April 24, 1914, he had a slight attack of the "old giddy sensations." When seen on May 3, 1914, the skin rashes had disappeared and the gumma on the right shin was no longer evident. All the areas of tenderness had disappeared, and he no longer complained of the "rheumatics." He was not subject to any headaches and his scalp was no longer tender. Hearing had improved and the signs of left-sided deafness were no longer demonstrable. The fundi appeared natural and the reaction of the pupils was normal. Ataxy and Romberg's sign were not present. He walked well. The plantar reflexes now gave flexor responses and all the other reflexes were normal. His wife said that he was no longer irritable and passionate, and that his temper was equable; that in fact he was now "a different man, quite like his old self."

On May 7, 1914, he was injected with another dose of 0·9 grm. of neosalvarsan; and on June 17, 1914, his Wassermann reaction was serum 4.4.4.0.0. c.s.f. 0.0.0.0.0.

## § 4.—*Muscular Atrophy.*

When we consider the nature of the changes produced in the spinal meninges by the activity of the syphilitic virus, it is obvious that the anterior nerve-roots must suffer, as their fibres are leaving the spinal cord. Muscular atrophy must consequently occur from time to time as a natural result of syphilis meningo-vascularis. We have already given an instance of such a lesion affecting both posterior and anterior nerve-roots, and causing loss of sensation and muscular wasting in one leg (No. 60, p. 20). Occasionally, however, the anterior roots alone are affected and, if the muscular atrophy occupies the upper extremity, it is usually spoken of as syphilitic amyotrophy.

Now the nature of muscular atrophy in syphilitic persons has been the subject of much discussion; but Léri [7] and others have amply demonstrated the existence of a progressive amyotrophy due to meningo-vascular changes of syphilitic origin.

But the cause of progressive muscular atrophy associated with signs

of tabes dorsalis stands on a less certain footing, and we shall therefore consider the views of the various authorities on syphilitic amyotrophy more fully in the chapter on syphilis centralis (p. 109). Meanwhile we give an instance characteristic of that form of muscular atrophy due to spinal meningitis and its associated vascular changes. In this patient [No. 36] other signs of active syphilis were apparent in the central nervous system, in addition to the muscular atrophy; for not only had she suffered from a prodromal headache and a "stroke," in which she lost her speech for a time, but her pupils reacted badly to light, there was slight weakness of the left half of the face, and ankle-clonus, together with an extensor plantar response, was obtained from both feet. She also had difficulty in holding her water, and could not control her motions if they were soft.

*A Case of Muscular Atrophy of both Upper Extremities, with signs of Pyramidal Interference. Positive Wassermann Reaction in the Cerebro-spinal Fluid. History of previous Cerebral Affection.*

*Case* 36.—R. C., female, married; born 1876. She was married in 1900, at the age of 24, but left her husband three years later, because he would not work. No definite history of syphilitic infection was obtained. She had never been pregnant.

In 1909 she suffered for four weeks from intense headache, which ultimately passed away entirely.

In December, 1910, she had a "stroke"; her speech became affected, and she was unable to walk steadily. Since then her memory had deteriorated, and she had been unable to work.

In January, 1912, her right hand began to waste, and she lost power so rapidly that, by June of the same year, she was unable to hold a knife. This wasting was thought at another hospital to be due to cervical ribs, and in July a rib was removed, but she steadily grew worse. In September the left hand became affected. Ever since the middle of 1912 occasionally she had been unable to control her motions or hold her water.

In November, 1912, she was admitted to the London Hospital under the care of Dr. F. J. Smith. Her speech was slurred. She suffered from no headache, and had not been subject to attacks of vomiting.

The pupils reacted to light, but the contraction was not maintained, and tended to be rhythmic; the reaction was normal on accommodation. The eyes moved well. Her face was expressionless, and there was slight weakness of the lower portion on the left side. The tongue moved well, and was not tremulous. Movements of the jaws, palate, and larynx were normal.

Smell, taste, hearing, and vision were unaffected, and the fundi showed no abnormal appearances.

All the muscles of both hands, of both forearms, and to a less degree of the arms, were considerably wasted, especially on the left side. The muscles

of the shoulder-girdle were much less affected. Both lower extremities were slightly spastic.

No hyperalgesia or loss of sensation could be discovered, even in the arms.

The knee-jerks were exaggerated, ankle-clonus was obtained on both sides, and both plantar reflexes gave an extensor response. The abdominal reflexes were unaffected.

She had considerable difficulty in holding her water, and could not control her motions if they were soft.

There was some osteo-arthritis of the right shoulder, elbow, and wrist.

No abnormal signs were discovered in the heart, lungs, or abdomen, and the urine contained neither albumen nor sugar.

On November 28, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.2.}{\text{es.f.} \quad 4.4.1.0.0.}$

Such a case exactly fits in with the description given by Léri [7] and Léri and Lerouge [9] of cases of muscular atrophy due to meningo-vascular changes, in two of which a microscopical examination was carried out.

But in the next case (No. 146) the signs were much less extensive; the pupils reacted well, the plantar reflexes were normal and the sphincters unaffected. The astonishing recovery under treatment and the simultaneous change in the strength of the Wassermann reaction in the cerebrospinal fluid show, however, that the case was one of syphilis meningo-vascularis amyotrophica.

*A Case of Muscular Atrophy of the Right Upper Extremity with no other gross signs of Nervous Disease. Strongly Positive Wassermann Reaction in the Cerebrospinal Fluid.*

*Case* 146.—M. S., female, married; born 1885. In July, 1910, soon after the birth of her last child, she began to lose power in the right thumb and hand; within the space of one year all the muscles of the right forearm and hand had become wasted, and she was unable to use this hand for grasping. For the first twelve months after the onset of this wasting, pain was not a noteworthy feature, but in October, 1911, she began to complain of severe pains in the back of the neck, shooting down the affected limb.

No history of syphilitic infection could be obtained; but in 1904, shortly after marriage at the age of 19, she suffered from "anæmia and indigestion." Her husband died in an Asylum of "dementia paralytica" in June, 1912. The first child of this marriage was born in 1904 and died three months later of "wasting;" the second born in 1905 survived and is healthy; the third was born in 1907 and the fourth in May, 1910. The child born in 1910 gives a negative Wassermann reaction in the serum.

On admission to the London Hospital in March, 1912, there was grave weakness and wasting of the right upper extremity. She was unable to grasp

small objects with her right hand. The right wrist was dropped and the extensor muscles of the right fingers and thumb were extremely paretic; the flexor muscles were less affected than the extensors. All the small muscles of the hand, the interossei, the thenar and hypothenar muscles, were intensely wasted. The muscles around the right shoulder-joint were fairly developed. The small muscles of the right hand and the extensor muscles of the right forearm did not react to the interrupted current; to galvanism they responded with a characteristically slow contraction. The left upper extremity was completely unaffected. Her gait was natural and her legs showed neither wasting nor spasticity.

She complained of severe dragging and shooting pains in the back of the neck and along the right forearm; but, on testing, no disturbance of sensibility could be discovered anywhere.

The knee-jerks were brisk and ankle-jerks were readily elicited. The abdominal reflexes were easily obtained and both plantar reflexes gave a flexor response.

Mentally she was depressed and worried, but her memory and attention were good. She complained of no headache and there was no tenderness of the scalp. She had suffered neither from seizures nor from attacks of vomiting.

All ocular movements were well performed. The pupils reacted briskly to light and accommodation. The face was flattened and expressionless. The tongue showed no fibrillary tremors. The movements of the palate and larynx were unaffected. Vision and the optic discs and fundi were unaffected; smell, hearing and taste were normal.

At no time had she experienced any difficulty in holding or passing her water.

On April 24, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.4.2.}$ and the cells numbered 10 per cubic millimetre.

On July 29, 1912, she was injected with 0·9 grm. of neosalvarsan, and on August 1 this dose was repeated. After the injections her mental state brightened, the pains in the neck ceased and power in the right upper extremity began to return.

On November 27, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.3.2.0.}{\text{cs.f. } 4.1.0.0.0.}$ and the cells numbered 20 per cubic millimetre.

On November 30, 1912, she was given another dose of 0·9 grm. of neosalvarsan.

About Christmas, 1912, she again became pregnant, and on September 20, 1913, was delivered of a healthy male child.

On December 3, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.1.0}{\text{cs.f. } 4.0.0.0.0.}$ and the cells numbered 1 per cubic millimetre.

On December 4, 1913, she was again injected with 0·9 grm. of neosalvarsan.

In May, 1914, the extensor muscles of the right forearm had regained their normal size and power and the grasp of the right hand was as powerful as that of the left, but the muscles of the first interosseous space were still small and paretic.

Thus we agree with Léri that one form of spinal amyotrophy is certainly due to the meningo-vascular changes of syphilis; we can confirm his statements that the atrophy is liable to be accompanied or preceded by pains of root-origin, and that the reactions of the pupil may be disturbed. We also agree that there is considerable lymphocytosis in the fluid from the lumbar sac, and would add that, in these cases, the Wassermann reaction is positive in the cerebrospinal fluid if the patient has not been treated with mercury or intravenous injections of the arsenic compounds.

We believe, however, that there is another group of cases where the disease, though of syphilitic origin, progresses uninfluenced by treatment. Such a condition is exactly analogous to tabes dorsalis and will be dealt with in Chapter V, where we discuss syphilis centralis (*vide* p. 109).

### § 5.—*Myelitis.*

There is no period after infection when the patient may not be attacked with a paraplegia, showing all the symptoms and signs of a more or less complete transverse lesion of the spinal cord; this is usually spoken of as syphilitic "myelitis" or "meningo-myelitis." It is not uncommon in the secondary stage and may be accompanied by a rash upon the body and mucous patches of the mouth and anus. But an exactly similar set of signs and symptoms of intraspinal disease may appear many years after infection. From the neurological aspect, there is no obvious difference between the clinical manifestations at the different "stages." In all cases the essential signs are those of meningitis accompanied by more or less vascular disturbance.

The pathology of this "meningo-myelitis" has been fully worked out by innumerable observers (cf. Nonne [13], p. 377 *et seq.*); the lesion consists of inflammatory infiltration of the meninges and spinal nerve-roots accompanied by a variable amount of destruction of the spinal cord, secondary to a disturbance of its blood-supply. It is in fact a characteristic meningo-vascular condition.

Perhaps the commonest clinical manifestations produced by such a lesion are spastic paralysis, with or without a girdle sensation; spasticity with ataxy is also extremely frequent and occasionally this variety of the disease produces a more or less perfect form of Brown-Séquard paralysis. But in this case the signs of pyramidal affection are always bilateral, however completely the sensory manifestations may follow the Brown-Séquard type.

In cases of "meningo-myelitis" micturition tends to be disturbed early in the course of the disease, and some difficulty in passing the water may form one of the earliest symptoms (cf. No. 19, p. 27).

The cerebrospinal fluid from these patients tends to yield an extremely positive Wassermann reaction; but this can usually be profoundly affected by treatment. Thus in No. 134 and also in No. 10, who had been under treatment previously with mercury, it became entirely negative.

The final result, however, from the patient's point of view, depends on the amount of secondary destruction of tissue which has occurred in consequence of vascular occlusion or diminished blood-supply.

*A Case of so-called "Myelitis," with a Positive Wassermann Reaction in the Cerebrospinal Fluid, which became greatly reduced in strength within Four Months of Treatment.*

*Case* 134.—G. R., male, married, naval tailor: born 1874. This patient joined the Navy at the age of 21, and remained in good health until he caught syphilis in October, 1910, at the age of 36. He suffered from a chancre on the penis, which was followed by the development of adenitis, anæmia, a rash, and condylomata. He was treated at the Royal Naval Hospital, Chatham, with eight injections of mercury, and then took mercurial pills for fourteen months until January, 1912.

On January 6, 1912, after a period of ill-health, in which he complained chiefly of headaches and giddiness, he had a seizure which was followed by the development of a right-sided hemiparesis. On January 9, 1912, he was admitted to the Chatham Hospital, and was treated with mercury and iodides by the mouth. On March 7, 1912, he was discharged from hospital apparently cured.

On June 1, 1912, the left leg became affected; this was followed by retention of urine, pains in the back and abdomen, and later by a complete inability to move both legs.

On June 13, 1912, he was admitted to the London Hospital. The general aspect of the patient somewhat resembled that of a case of congenital syphilis. The nasal bridge was greatly depressed, the hair was receding, but the teeth were not pegged, and no scars were seen around the angles of the mouth. Pigmented scars were present on the front of both shins, and there was a scar on the penis.

His attention and memory were impaired. He complained of intense general headache, accompanied by pressure tenderness of the scalp and of dreams and "frights" by night. He had suffered from a seizure on January 6, 1912, but had not been subject to attacks of vomiting. His speech was slurred and mentation slow. Vision and the fundi were unaffected. He was deaf in both ears: tests showed that both internal ears were affected, the right more so than the left. Smell and taste were normal.

All movements of the eyeballs were badly performed, but there was no actual paralysis of any external eye-muscle. The pupils were equal, and reacted normally. The other cranial nerves were unaffected.

He could just move both legs; the power at the right hip was greater than that at the left: he could not move the toes or ankles either on the right or on the left side. In action the hands were clumsy and paretic, and the grasps were feeble. Alignment of the fingers was defective: closure of the eyes caused the outstretched hands to fall away, and diminished the power of his grip. The lower abdominal muscles and the lower portion of the erector spinæ were completely paralysed. All the muscles below the umbilicus were flaccid.

All forms of sensibility were gravely defective below the level of the distribution of the eighth thoracic roots on both sides. Sensation to light touch, and to heat, cold, and pain were impaired, but nowhere completely lost. He could not appreciate the vibrations of a tuning-fork below the level of about the ninth ribs, and was unable to recognize posture and passive movements in both legs. Over both upper extremities sensibility to touch, pain, and temperature was not impaired, but recognition of posture and passive movement was poor, and the length of time during which the vibrations of the tuning-fork were appreciated was relatively shortened.

The right knee-jerk was extremely brisk, the left was readily obtained. Ankle-clonus could not be elicited. On both sides the plantar reflexes gave an extensor response. The abdominal and cremasteric reflexes were completely abolished. The wrist- and elbow-jerks were obtained.

He was unable to pass urine, and suffered from retention with overflow. This was complicated with a stricture of the urethra and cystitis. The Wassermann reaction on June 19, 1912, was $\frac{\text{serum } 4.4.4.4.0.}{\text{cs.f.} \quad 4.4.4.4.4.}$

He was given 0·6 grm. of salvarsan on June 28, 1912, and 0·9 grm. of neosalvarsan on July 21, 1912, and on October 8, 1912; on the last date the Wassermann reaction was $\frac{\text{serum } 4.2.1.0.0.}{\text{cs.f.} \quad 4.2.0.0.0.}$

On July 19, 1914, he was readmitted to the Hospital. The physical signs were little altered but his general condition was greatly improved, and he could now do his work as a tailor.

On July 22, 1914, the Wassermann reaction was $\frac{\text{serum } 2.0.0.0.0.}{\text{cs.f.} \quad 0.0.0.0.0.}$ and the cells numbered 2 per cubic millimetre.

*A Case of Brown-Séquard Paralysis where a Positive Wassermann Reaction in the Cerebrospinal Fluid became Negative under Treatment.*

*Case* 10.—C. B., male, single, pawnbroker's assistant; born 1870.

He denied all venereal infection; but in August, 1908, a typical gumma of the forearm appeared and healed rapidly on the administration of iodides.

On June 1, 1911, he began to complain of tightness across the upper abdomen. The pains continued off and on until August 17, 1911, when he found that he could not pass his water; complete retention of urine developed,

necessitating the use of a catheter, and on August 21, 1911, he was admitted to the London Hospital.

On admission he complained of boring pains in the head accompanied by pressure tenderness of the skull. His mental state was little affected. Speech was natural. He had never complained of vomiting. No abnormal signs were discovered in the territory of the cranial nerves.

There was complete flaccid paralysis of the left leg and grave weakness of the right. The arms were unaffected.

He complained of spontaneous shooting pains in the upper part of the chest on both sides over the areas supplied by the third to the sixth thoracic nerve-roots and over this region of the trunk hyperalgesia was present to the dragged point of a pin. Below the hyperalgesic zone on both sides there was much loss of sensation to the prick of a pin, painful pressure, and to the hot and cold tubes. This loss was greater on the right leg than on the left. To passive movement and the vibration of a tuning-fork there was also considerable loss of sensibility, greater on the left leg than on the right. Appreciation of touches with cotton-wool was less affected on both legs than any other form of sensibility.

The knee-jerks on both sides were exaggerated, more so on the left than on the right. Ankle-clonus was readily obtained on the left side and was less definite on the right. The plantar responses on both sides were extensor. The lower abdominal reflexes could not be elicited, the upper ones were brisk. The wrist- and elbow-jerks were normal.

There was complete retention of urine with overflow and an inability to hold the motions when soft.

Between August 28 and October 4, 1911, he was treated with thirty-six inunctions of mercury and the weakness of the legs improved rapidly.

On June 6, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.1.0.}{\text{cs.f.} \quad 4.1.0.0.0.}$

On July 22, 1912, he was injected with 0·6 grm. of salvarsan, and on July 27, 1912, with 0·9 grm. of neosalvarsan.

On July 2, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.1.0.}{\text{cs.f.} \quad 0.0.0.0.0.}$ and the cells numbered 1 per cubic millimetre.

On June 28, 1913, he was again injected with 0·9 grm. of neosalvarsan, and on December 4, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.0.0.0.}{\text{cs.f.} \quad 0.0.0.0.0.}$ and the cells numbered 2 per cubic millimetre.

Since November, 1911, his physical condition has remained stationary. In January, 1914, he showed spastic paralysis of the left leg, with profound loss of appreciation of vibration and of posture. Sensibility to pain, heat and cold was greatly diminished over the right lower extremity. But, like so many of these cases of Brown-Séquard paralysis of syphilitic origin, ankle-clonus could be obtained on both sides and both plantar reflexes gave an extensor response. His sphincters were controlled with difficulty.

## § 6.—*Lateral and Combined Degenerations.*

Not infrequently meningo-vascular syphilis produces clinical manifestations closely resembling those due to primary degeneration of the long tracts of the spinal cord. The patient suffers from spasticity, with or without ataxy, and no girdle sensation or root-area is present to indicate the focal level of the lesion. But such cases differ from those of primary degeneration of the lateral and posterior columns of the spinal cord in the effect produced by treatment on the positive Wassermann reaction in the cerebrospinal fluid. From strongly positive it may become negative, and at the same time the symptoms may improve considerably; but as the essential lesion is frequently a secondary degeneration, consequent on slow vascular occlusion, the improvement is less than in many cases of apparently severe "meningo-myelitis."

We have chosen No. 91 to illustrate this condition because, in addition to the signs of interference with the pyramidal tracts, he had an area of radicular hyperalgesia and transitory difficulty in micturition, showing that the lesion in these cases is closely akin to that in "meningo-myelitis."

He also illustrates remarkably well the change that can be produced in the Wassermann reaction of the cerebrospinal fluid by effective treatment.

*A Case of "Meningo-myelitis" accompanied by a Gumma of the Palate. Positive Wassermann Reaction in the Cerebrospinal Fluid which became Negative under Treatment. Appearance of Herpes Zoster over the Second Cervical Area.*

*Case* 91.—D. K., male, married, labourer; born 1878. In 1904, at the age of 26, he contracted syphilis and suffered from a chancre, rash and sore throat, for which he was treated with mercury by the mouth for twelve months.

In 1907 he developed gummatous ulcers on his shins which healed rapidly on the administration of iodides.

On January 4, 1912, he was taken ill with dizziness, pains in his abdomen and repeated vomitings. This attack was followed by headache, which lasted until his admission in July, 1912.

About four weeks before his admission a pimple appeared on his palate which enlarged, broke down and led to a perforation into the nose.

On admission to the London Hospital in July, 1912, all the cerebral functions were unimpaired; speech and memory were unaffected. He had not suffered from seizures but complained of severe, general, gnawing pains in the head accompanied by soreness of the scalp and tenderness on pressure. The pains were constantly present, but were always worse at night. From time to time before admission he had suffered from attacks of retching,

flatulence, abdominal distension, pyrosis and even actual vomiting. The special senses were unaffected.

Movements of the eyes, face, tongue, palate and larynx were unimpaired, and the pupils reacted normally.

He walked well and was not ataxic. Both great toes tended to remain in the extended posture, although there was no noticeable increase of tone in the muscles of the lower extremities, and no loss of muscular power.

Distinct tenderness and hyperalgesia were present in the region of the eighth and ninth thoracic nerve-roots on both sides, but no sensory change could be discovered elsewhere to any test.

The knee-jerks and ankle-jerks were exaggerated and both plantars gave an extensor response. The upper abdominal reflexes were brisk and the lower ones could just be obtained.

He had a little difficulty in beginning micturition, but no other sphincter trouble.

A small perforation was seen at the back of the hard palate leading from the mouth to the nose. No abnormal signs were discovered in the heart, lungs, abdomen or urine.

On July 10, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.3.0.0.}{\text{cs.f. } 4.4.4.1.0.}$

He was given 0·6 grm. of salvarsan on July 10, 1912, and a similar dose on the 17th. By January 15, 1913, the reaction had become $\frac{\text{serum } 3.2.1.0.0.}{\text{cs.f. } 1.0.0.0.0.}$ At the same time the headache and the hyperalgesia around the trunk disappeared and his general condition improved strikingly.

On January 15, 1913, he was given 0·9 grm. of neosalvarsan. To this dose there was no provocative increase in the strength of the Wassermann reaction in the serum, for on January 22, 1913, the reaction was $\frac{\text{serum } 3.2.1.0.0.}{\text{cs.f. } -.-.-.-.-.}$ and this remained at about the same strength until June, 1913. On June 6, 1913, the reaction was $\frac{\text{serum } 3.2.1.0.0.}{\text{cs.f. } -.-.-.-.-.}$ When, however, this patient was seen on June 25 he showed a typical herpetic eruption on the supply of the second cervical root, on the right side, and at the same time the reaction had increased to $\frac{\text{serum } 4.3.0.0.0.}{\text{cs.f. } -.-.-.-.-.}$ At this time he received no further antisyphilitic treatment and yet on August 26, 1913, the reaction was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } -.-.-.-.-.}$ but on November 12, 1913, it had again risen to $\frac{\text{serum } 4.1.0.0.0.}{\text{cs.f. } -.-.-.-.-.}$ without the appearance of any fresh manifestations.

## § 7.—*Epilepsy.*

It is generally recognized that diffuse changes in the cerebral meninges of syphilitic origin may produce a condition indistinguishable

from idiopathic epilepsy. We are not concerned here with a localized gummatous meningitis and its Jacksonian attacks, but with a more diffused lesion associated with recurrent loss of consciousness and general convulsions (cf. Nonne [13], p. 141).

It is obvious that idiopathic epilepsy may occur in a man who has been affected with syphilis and yet the two conditions may not be in any way connected pathologically. But, on the other hand, there can be little doubt that a condition, clinically indistinguishable from epilepsy, may occur as the direct result of syphilis. With a positive Wassermann reaction in the serum and a negative one in the cerebrospinal fluid, it is, however, impossible to be certain of such a diagnosis unless some other physical sign points to the organic nature of the lesion.

We have, therefore, chosen No. 303 and No. 207 as our examples, because in both cases the defective reaction of the pupils pointed to something more than idiopathic epilepsy. At the same time the negative reaction in the cerebrospinal fluid makes it unlikely that they are instances of Fournier's "parasyphilitic epilepsy" ([4], p. 238), or, as we should prefer to call it, syphilis centralis with epileptiform attacks (*vide* Chapter V, § 6, p. 121).

Both these patients illustrate the general mental disturbance so commonly associated with attacks of syphilitic epilepsy. Thus in No. 303 the first seizure was followed by a period of confusion lasting at least twenty-four hours, and No. 207 usually remains "dazed" for many hours after waking from his post-convulsive sleep. He also illustrates the extreme difficulty in preventing the fits by means of bromides; this drug somewhat diminishes the severity and frequency of the attacks, but does not produce that improvement we should expect in a case of idiopathic epilepsy.

*A Case of Epileptiform Convulsions, associated with Defective Reaction of the Left Pupil and Loss of the Ankle-jerks. Negative Wassermann Reaction in the Cerebrospinal Fluid.*

*Case* 303.—A. S., male, single, tramcar driver; born 1879. In 1900, at the age of 21, he contracted syphilis and suffered from a sore on the penis and a discharge from the urethra which were followed by a bubo in the right groin, but no manifestations of secondary syphilis; he was treated for a few weeks only.

Early in 1911 he became very sleepy; after driving his tram for some time he would come home and immediately fall asleep; whilst driving he often felt sleepy, but never actually fell asleep on the car. Shortly after this he became subject to severe headaches.

On January 17, 1912, about 7 p.m., he was in charge of his car when he

ran into a barrow; he just touched the barrow, but no damage was done. Fifteen minutes later he "came over dazed," stopped the car and immediately fell forward. He was taken to the London Hospital and admitted in a dazed, semi-conscious condition; he could hardly speak and misused words; he moaned and wept bitterly. On his arrival in the ward he was excited, restless and difficult to manage. He remained an in-patient until January 19, 1912, and on discharge seemed perfectly normal. No gross manifestations of disease were discovered.

He then remained in fair health until June, 1912, when he had an epileptiform attack in the street, lost consciousness and was carried home; an hour later he came to himself. He was then free from seizures until December, 1912; on the 15th of that month whilst sitting reading in front of the fire he lost consciousness and fell into the fireplace. The fourth attack occurred in September, 1913; he was walking in the street about 7 p.m. when he was seized with a sharp shooting pain in the head; he felt drowsy, sat down on the pavement and then "struggled" and lost consciousness. Between September, 1913, and January, 1914, when he first came under our observation, he had four or five small fits. On January 20, 1914, an attack came on without warning and was much more severe and lasted much longer; he was unconscious for two hours, became extremely violent, was cyanosed, bit his tongue and passed his water. On February 20 he had a slight attack.

He stated that since his first seizure his memory had become defective. In 1912 he had been subject to attacks of headache, but he had never vomited nor experienced any feelings of nausea. At no time had he suffered from any pains in the extremities or trunk. He had not lost his skill with his hands and motion had never been affected.

On his admission to the London Hospital on March 16, 1914, his mental state was unaffected, his attention good. He slept normally. Memory to ordinary tests was unaffected and no suggestions of dementia were present.

His speech was natural, and hearing, smell, taste and vision normal. The optic discs and fundi appeared healthy. All ocular movements were well carried out. The pupils were equal, well centred, and regular in outline: the left pupil did not react to light but reacted well to accommodation, the right reacted briskly both to light and to accommodation. The expression of his face was normal. Movements of the jaw, palate, larynx and tongue were unimpaired. Motion, sensation and the action of the sphincters were completely unaffected. The knee-jerks were natural, but both ankle-jerks were abolished. The wrist- and elbow-jerks were normal and the abdominal reflexes brisk. Both plantar reflexes gave a flexor response. No abnormal signs were discovered in heart, vessels, lungs, abdomen or urine.

On March 18, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.2.0.}{\text{cs.f.} \quad 0.0.0.0.0.}$ and the cells numbered 2 per cubic millimetre. He was injected with doses of 0·9 grm. of neosalvarsan on March 18, March 20, and March 22, 1914. On April 22, 1914, he had a slight fit, and since that time has remained free from attacks (July, 1914), and his general health has improved greatly.

*A Case of Epileptiform Seizures with Defective Reaction of the Pupils. Negative Wassermann Reaction in the Cerebrospinal Fluid.*

*Case* 207.—F. W., male, married, labourer; born 1871. In 1892, at the age of 21, this patient contracted a hard chancre, followed by recurrent sore throat, fall of hair and anæmia; he was treated with mercury by the mouth for two years.

In 1897 he married. His first child, born in June, 1897, gives a positive Wassermann reaction in the serum, and shows the characteristic features of congenital syphilis. Five miscarriages followed this pregnancy; the next living child was born in 1903, and children born in 1908 and 1912 also survive.

After marriage he drank heavily. During the years 1901, 1902 and 1903 he was constantly ailing; he complained chiefly of his head, due, as he thought, to alcoholic excess. One hot day in June, 1903, whilst at work on a scaffold, he was seized with a severe left-sided headache, and about half an hour later had his first "fit." In this attack he lost consciousness and wetted himself. After this he suffered from a severe dull headache and completely lost his sense of taste. At this time he was in bed for seven days and away from work for a fortnight. From July, 1903 until the beginning of 1905 he attended the London Hospital as an out-patient and was treated with bromides for "epilepsy." At first the fits came on about once a week, but under treatment the frequency and severity of the attacks diminished. About October, 1904, he began to complain of attacks of pain in the chest, "a tightness and a feeling as if knives were being inserted into the skin." From October, 1904, until January, 1905, he had an attack of this sort almost every day. In the years 1906, 1908 and again in 1912 he suffered from "shooting rheumatic pains" in the back of the thighs and the inner side of the legs and feet. In 1911 he ceased to take bromides and gradually the fits became more severe and more frequent. In 1912 he also complained at various times of pains shooting down the inner side of the right arm and forearm, and in the right axilla, and later in the same year was much troubled with "sciatica" in the back of the thighs and calves. From time to time between the years 1895 and 1913 he complained of "soreness of the mouth with ulceration."

The fits were characteristically epileptiform. They came on at any time by day or night. Usually a seizure occurred about once a fortnight, but frequently the attacks would come on in groups of three or four. Before the seizure he felt "full and muzzy," and he knew that a fit was hanging about him because he lost his taste. In each attack he became unconscious and cyanosed; he usually passed his water and frequently bit his tongue. In the attack he said that he "felt a sort of pain creeping up the limbs, more especially on the right side, then a tingling in the left eye and the left side of the face, next his sight became dim, he heard distant noises in his ears and then he lost himself." In the attacks, which occurred whilst he was under observation, his head was seen to turn to the left and, before the convulsion became generalized, he closed his left fist tightly. After the

attacks he was dazed and drowsy for some hours, and, if alone, usually slept. He said that alcoholic excess would always bring on the fits, and that they occurred more frequently when he was worried or away from work.

He complained of attacks of headache in the frontal and vertical regions passing into the back of the neck: when the headache came on the vision of the left eye was always affected. In 1903 he had been subject to attacks of nausea and vomiting, but after that year he rarely vomited.

On admission to the London Hospital in June, 1913, his speech was slow and his articulation defective, but there was no slurring of syllables. His memory was bad. He did not know the year of his birth and could not calculate back to the date of his marriage. He knew the value of money, but had forgotten his multiplication tables. He was unable to remember any details of events which had happened more than a few weeks before his admission. Mentation was slow, but his answers to questions were accurate and rational. He was nervous, irritable and inattentive. He boasted freely, but had no grandiose ideas. Delusions and hallucinations were absent.

Hearing was not affected, smell was poor and before each fit he completely lost all sense of taste; this returned in part after the attack had passed off. Vision and the visual fields were not grossly affected, and the optic discs and fundi appeared natural.

All ocular movements were well performed. The pupils were small, well centred and regular in outline; neither reacted to moderate illumination, but both reacted sluggishly to strong lights and well to accommodation. The movements of the face, jaws, palate and tongue were unaffected. The gait was natural and all co-ordinated movements were well carried out.

He complained of no spontaneous pains, but over the front and back of the chest, within an area corresponding to the distribution of the third, fourth, fifth, and sixth thoracic roots on both sides, pricks were said to be "less sharp" and "less localized," and the sensation evoked by the hot and cold tubes seemed "less hot" or "less cold" than elsewhere over the body. To pinching of the skin and the dragged point of a pin the skin around the right shoulder-joint was tender. There was no sensory loss to posture, passive movement, the vibrations of a tuning-fork, cotton-wool, heat and cold elsewhere on the extremities or trunk.

Osteo-arthritic grating was present in the right shoulder-joint and the patient complained of pain when this joint was moved.

The knee- and ankle-jerks, and the abdominal and plantar reflexes all gave normal responses, and the sphincters were controlled.

The tongue was deeply fissured and a scar was present on the penis. The teeth were notched and much worn, the nasal bridge was depressed but no scars were seen at the angles of the mouth.

No abnormal signs were discovered in the heart, lungs, abdomen or urine.

On June 6, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.3.0.}{\text{cs.f.} \quad 0.0.0.0.0.}$ and the cells numbered 2 per cubic millimetre.

On June 13, June 19 and June 26, 1913, he was injected intravenously with doses of 0·9 grm. of neosalvarsan. After the first two of these injections he had three epileptiform attacks exactly resembling those described above.

### [B] The Wassermann Reaction in Syphilis Meningo-vascularis.

It was generally held that the cerebrospinal fluid gave a negative reaction in syphilitic affections of the central nervous system, and that this was an important aid in differential diagnosis between such conditions and "parasyphilis," where the reaction was overwhelmingly positive. This view was expressed by Plaut as late as 1913 [19] and by Mott in his first communication to the International Medical Congress [11]; subsequently, however, Mott somewhat modified his statement, [12]. In 1912 Nonne stated that the cerebrospinal fluid is not usually positive except with the larger volume of fluid used in the "Auswertungsmethode" of Hauptmann and Hössli; then, however, it is always positive. Later, before the International Medical Congress in 1913, Nonne [14] summed up his views on this subject in the following statement: "Auch das Verhalten der W.-R. bei Tabes und Paralyse und bei den atypischen syphilogenen Rückenmarkserkrankungen lässt seit der Einführung der Hauptmannschen Auswertungsmethode einen *prinzipiellen* Unterschied gegenüber den echt luetischen Erkrankungen des Nervensystems nicht erkennen."

But early in this research [10] we were led to believe that the character of the Wassermann reaction in the cerebrospinal fluid, in cases of meningo-vascular syphilis, depended mainly on the site of the lesion. If the signs and symptoms pointed to an affection of the spinal cord, its membranes or nerve-roots, the reaction was usually positive in the cerebrospinal fluid, and the strength of this reaction was often as great as that in any other condition of syphilitic origin.

But the more completely the clinical manifestations were confined to some affection of the cerebrum or its vessels, the more often was a negative reaction obtained in the cerebrospinal fluid. Even when a positive reaction was present, it was relatively feeble and usually transitory.

Between the cerebrum on the one hand and the spinal cord on the other stands the behaviour of the reaction with affections of the cranial nerves, produced by meningo-vascular syphilis. Sometimes the cerebrospinal fluid gives a positive, sometimes a negative reaction, according to the extent and situation of the signs and symptoms [cf. p. 49].

INCIDENCE OF THE WASSERMANN REACTION IN SYPHILIS MENINGO-VASCULARIS.

TABLE A.—*Cases in which the Contents of the Spinal Canal were apparently affected.*

| No. of case | Result of first examination | No. of case | Result of first examination |
|---|---|---|---|
| 3 (p. 34) | serum 4.4.4.4.4.<br>cs.f. 4.4.4.3.2. | 175 | serum 4.4.4.4.4.<br>cs.f. 4.4.4.4.2. |
| 10 (p. 71) | 4.4.4.1.0.<br>4.1.0.0.0. | 177 | 4.4.4.4.4.<br>4.4.4.4.0. |
| 19 (p. 27) | 4.4.4.4.4.<br>4.4.4.3.2. | 189 (p. 60) | 4.4. . . .<br>4.4.4.0.0. |
| 26 | 4.4.4.4.4.<br>4.4.4.0.0. | 201 | 4.4.4.4.4.<br>4.4.4.4.4. |
| 36 (p. 66) | 4.4.4.4.2.<br>4.4.1.0.0. | 202 | 4.4.4. . .<br>4.3.0.0.0. |
| 45 | 4.4.4.4.4.<br>4.4.4.4.4. | 217 | 4.4.4.4.0.<br>4.4.4.4.0. |
| 59 (p. 37) | 4.4.4.4.4.<br>4.4.4.4.3. | 226 (p. 46) | 4.4.4.4.1.<br>4.4.3.0.0. |
| 60 (p. 20) | 4.4.4.4 4.<br>4.4.3. . . | 228 | 4.4.4.4.4.<br>1.0.0.0.0. |
| 64 | 4.3.2.0.0.<br>4.4.4.3.1. | 235 | 4. . . . .<br>4.4.2.0.0. |
| 74 (p. 51) | 4.4.4.4.3.<br>4.4.4.3.1. | 236 | 4.4.4.4.2.<br>0.0.0.0.0. |
| 77 | 4.4.4.4.4.<br>4.4.4.3.0. | 237 | 4.4.4.4.3.<br>4.4.4.4.4. |
| 86 (p. 44) | 4.4.3.3.0.<br>4.4.4 4.0. | 239 | 4.4.4.4.0.<br>4.4.2.0.0. |
| 91 (p. 73) | 4.4.3.0.0.<br>4.4.4.1.0. | 244 | 4.4.4.3.0.<br>4.4.4.0.0. |
| 94 | 1.0.0.0.0.<br>4.4.4.3.0. | 255 | 4.4.4.1.0.<br>4.4.4.0.0. |
| 102 | 4.4.0.0.0.<br>4.3.1.0.0. | 256 | 4.4.4.4.1.<br>4.4.4.4.4. |
| 106 | 4.4.4.4.4.<br>4.4.0.0.0. | 262 (p. 62) | 4.4.4.4.4.<br>4.4.4.4.0. |
| 114 | 4.2.0.0.0.<br>4.4.4.4.4. | 273 | 4.4.4.4.3.<br>4.4.4.4.4. |
| 134 (p. 70) | 4.4.4.4.0.<br>4.4.4.4.4. | 277 | 4.4. .4.4.<br>4.4.4.4.4. |
| 146 (p. 67) | 4.4.4.4.4.<br>4.4.4.4.2. | 279 | 4. . . . .<br>4.4.4.4.4. |
| 147 (p. 22) | 0.0.0.0.0.<br>4.4.1.0.0. | 284 (p. 11) | 4.4.4.4.4.<br>4.4.4.4.0. |

| No. of case | Result of first examination | No. of case | Result of first examination |
|---|---|---|---|
| 296 | serum 4.4.4.3.0.<br>cs.f. 4.1.0.0.0. | 309 (p. 32) | serum 4. - - - -<br>cs.f. 4 4.4.0.0. |
| 305 | 4.4.4.4.4.<br>4.4.4.3.1. | 313 (p. 30) | 4.4.4.4.4.<br>4.4.0.0.0. |
| 308 | 4.4.4.4.4.<br>4.0.0.0.0. | | |

TABLE B.—*Cases in which the Intra-cranial Contents only were affected.*

| | | | |
|---|---|---|---|
| 11 | serum 4.4.4.4.0.<br>cs.f. 0.0.0.0.0. | 170 | serum 4.4.4.4.4.<br>cs.f. 4 4.0.0.0. |
| 15 | 4.4.4.4.0.<br>0.0.0.0.0. | 204 | 4.4.4.4.1.<br>0.0.0.0.0. |
| 39 | 4.4.4.4.4.<br>0.0.0.0.0. | 205 | 4.1.0.0.0.<br>0.0.0.0.0. |
| 53 (p. 40) | 4.4.4.0.0.<br>0.0.0.0.0. | 207 (p. 77) | 4 4.4.3.0.<br>0.0.0.0.0. |
| 62 | 4.4.2.0.0.<br>0.0.0.0.0. | 223 | 4.4.4.4.4.<br>0.0.0.0.0. |
| 73 | 4.4.4.4.0.<br>0.0.0.0.0. | 232 | 4.4. - - -<br>0.0.0.0.0. |
| 92 (p. 57) | 4.4.4.4.0.<br>0.0.0.0.0. | 240 (p. 48) | 4.4.4.4.4.<br>0.0.0.0.0. |
| 104 | 4.4.4.4.3.<br>0.0.0.0.0. | 253 (p. 53) | 4.4.4.4.4.<br>4.4.0.0.0. |
| 107 | 4.4.3.1.0.<br>4.2.0.0.0. | 269 | 4.4 [illegible] 2.0<br>0.0.0.0.0. |
| 110 | 0.0.0.0.0.<br>0.0.0.0.0. | 271 (p. 41) | 4.4.4.4.2.<br>0.0.0.0.0. |
| 111 | 4.3.1.0.0.<br>0.0.0.0.0. | 287 | 4.4.3.0.0.<br>0.0.0.0.0. |
| 122 (p. 16) | 4.4.4.4.4.<br>0.0.0.0.0. | 289 | 4.3.0.0.0.<br>0.0.0.0.0. |
| 128 (p. 56) | 4.4.4.4.4.<br>4.1.0.0.0. | 290 | 4.4.4.0.0.<br>0.0.0.0.0. |
| 133 | 4.4.4.4.4.<br>0.0.0.0.0. | 303 (p. 75) | 4.4.4.2.0.<br>0.0.0.0.0. |
| 149 (p. 58) | 4.4.4.4.2.<br>0.0.0.0.0. | 310 (p. 54) | 0.0.0.0.0.<br>4.1.0.0.0. |
| 158 | 4.4.4.4.4.<br>0.0.0.0.0. | | |

JUVENILE.

| No. of case | Result of first examination | No. of case | Result of first examination |
|---|---|---|---|
| 21 | serum 4.4.4.4.4.<br>cs.f. 3.0.0.0.0. | 85 | serum 4.4.4.4.4.<br>cs.f. 0.0.0.0.0. |
| 61 | 4.4.4.4.4.<br>0.0.0.0.0. | 156 | 4.4.4.4.2.<br>0.0.0.0.0. |
| 65 | 4.2.0.0.0.<br>0.0.0.0.0. | | |

But in order to show that this statement is, in the main, correct, every patient must be examined thoroughly on more than one occasion, and if possible by more than one observer. For an obvious cerebral lesion, which would not usually produce a positive reaction in the cerebrospinal fluid, may be complicated by a comparatively insignificant affection of the spinal meninges or roots; this will tend to induce a positive reaction, which, if unrecognized, may spoil an otherwise conclusive series of observations.

Even when care is taken in each case to note whether the parts within the spinal canal are affected or not, the signs are not of equal value in foretelling the probable nature of the Wassermann reaction. For in patients with cerebral syphilis signs may appear pointing to some affection of the spinal meninges so transitory and slight that we could scarcely expect them to affect the cerebrospinal fluid drawn from the lower end of the lumbar sac. It is, however, remarkable how often such indications of some spinal affection influence the reaction of the cerebrospinal fluid.

In a few instances, however, in spite of the strictest clinical examination, no signs could be discovered apart from those of disease of the cerebrum and its vessels, although the reaction was positive in the cerebrospinal fluid. But we must remember that in the Wassermann reaction we possess a means of investigation more delicate than any clinical method. On comparing the following tables, therefore, it is not surprising that they should contain exceptions to the rules we have laid down; the wonder is rather that in so many instances the clinical results should have coincided so closely with those of the Wassermann reaction.

Table A contains forty-five cases of meningo-vascular syphilis, where the clinical signs pointed to some affection of the spinal cord or its membranes, and in one only was the cerebrospinal fluid com-

pletely negative. This was the case of a young married woman (No. 236), who suffered from a meningo-myelitis below the level of the third thoracic segment. At the same time she bore the scars of gummatous ulcers on her shins, and belonged to the clinical group, in which a positive reaction is usually obtained in the cerebrospinal fluid.

Another case (No. 228) yielded so slight a reaction in the cerebrospinal fluid that it also should be classed as an exception; but as Fildes and McIntosh ([3], p. 228) pointed out, these faintly positive reactions may have no specific significance, or they may represent the last traces of a positive reaction in a fluid which is becoming negative. No. 228 subsequently developed root-lesions, and we were therefore obliged to include him under this heading; although at the time the first Wassermann reaction was obtained there were no definite signs pointing to an affection of the spinal meninges or vessels.

When we turn to Table B, containing thirty-six cases of cerebral lesions, the exceptions are more numerous; for it is much easier to obtain clinical evidence that the spinal contents are affected than to prove the opposite during life. It will therefore be well to consider more in detail these exceptional cases with a positive reaction.

No. 128 and No. 253 were both instances of cranial nerve paralyses, and, as we have already pointed out (p. 49), syphilis meningo-vascularis of the brain-stem is not infrequently associated with a positive reaction in the cerebrospinal fluid. Indeed, it is difficult to see how extensive basic meningitis could exist without some affection of the spinal meninges. In No. 128, a case of third nerve paralysis, the positive reaction became negative in the cerebrospinal fluid within six weeks of treatment. No. 253 was an instance of widespread signs of affection of many cranial nerves. Such patients usually give a positive reaction in the cerebrospinal fluid (*vide* p. 50).

In the same way, No. 107, although a case of left hemiplegia, showed some affection of the movements of the right half of the tongue, pointing in all probability to a meningo-vascular lesion of the brain-stem. To the same group belongs No. 310, an instance of Weber's syndrome; he suffered from complete paralysis of the left third cranial nerve with ptosis and a fixed pupil associated on the right half of the body with a hemiplegia of the arm and leg. Here also the reaction was a weak one, as is usual in those cases of meningo-vascular disease of the brain-stem, which give a positive reaction in the cerebrospinal fluid.

Thus, out of the five cases of cerebral syphilis, which gave a positive

reaction, four were suffering from some disease of the brain-stem, or its membranes, a condition liable to be associated with a weakly positive reaction in the cerebrospinal fluid.

Finally, in No. 170, a married woman suffering from right hemiplegia and dysarthria, we were unable, after careful examination in hospital, to find any signs of a lesion of the meninges and vessels of the spinal cord or brain-stem. In this case clinical methods failed to explain an apparent exception to our usual experience of the behaviour of the Wassermann reaction in the cerebrospinal fluid.

Of the five cases of juvenile syphilis of the brain, one yielded a weakly positive reaction, whilst all the others were completely negative.

Thus we have been able to show that in the case of meningo-vascular syphilis the key to the Wassermann reaction in the cerebrospinal fluid lies in the presence or absence of inflammatory changes in the meninges of the spinal cord and brain-stem. If they are affected, the reaction is positive, whilst, if they have escaped, the cerebrospinal fluid reacts negatively. Moreover, we have shown that in most cases careful clinical observation is able to detect signs which point to this affection of the meninges, and so enables us to foretell the character of the Wassermann reaction in the cerebrospinal fluid.

### [C] The Effect of Treatment on the Wassermann Reaction in Syphilis Meningo-vascularis.

Throughout the first part of this chapter we have insisted on the change in the Wassermann reaction of the cerebrospinal fluid which may be brought about in cases of meningo-vascular syphilis as the result of treatment, and we have described many instances where a strongly positive reaction became negative in the cerebrospinal fluid. But in order that this evidence may have its full value we have gathered together on Table C eighteen cases where the cerebrospinal fluid ultimately yielded a negative Wassermann reaction as the result of treatment. Fourteen of these cases have been fully described in the text on the page appended to the number in the first column.

In most cases this change was effected by three doses of 0·9 grm. of neosalvarsan, but in a few instances even relatively smaller doses of salvarsan were used. In all cases potassium iodide was given almost continuously throughout the period between the two Wassermann determinations.

TABLE C.—TO SHOW THE EFFECT OF TREATMENT ON THE WASSERMANN REACTION IN SYPHILIS MENINGO-VASCULARIS.

| No. of case | Before treatment | After treatment | Intervening period | Nature of treatment |
|---|---|---|---|---|
| 3 (p. 34) | 4.4.4.4.4.<br>4.4.4.3.2. | 4.4.4.4.1.<br>0.0.0.0.0. | 30 weeks | 3 doses of 0·9 grm. of neosalvarsan intravenously. |
| 10 (p. 71) | 4.4.4.1.0.*<br>4.1.0.0.0. | 4.4.4.1.0.<br>0.0.0.0.0. | 55 ,, | 1 dose of 0·6 grm. of salvarsan and 1 dose of 0·9 grm. of neosalvarsan intravenously. |
| 19 (p. 27) | 4.4.4.4.4.<br>4.4.4.3.2. | 4.4.4.4.3.<br>0.0.0.0.0. | 41 ,, | 1 dose of 0·9 grm. and 1 of 0·6 grm. of neosalvarsan intravenously. |
| 59 (p. 37) | 4.4.4.4.4.<br>4.4.4.4.3. | 4.4.1.0.0.<br>0.0.0.0.0. | 21 ,, | 4 doses of 0·9 grm. of neosalvarsan intravenously. |
| 60 (p. 20) | 4.4.4.4.4.<br>4.4.3. - - | 4.4.4.4.4.<br>0.0.0.0.0. | 49 ,, | 2 doses of 0·4 grm. of salvarsan intravenously. |
| 74 (p. 51) | 4.4.4.4.3.<br>4.4.4.3.1. | 4.4.4.3.0.<br>0.0.0.0.0. | 27 ,, | 3 doses of 0·9 grm. of neosalvarsan intravenously. |
| 86 (p. 44) | 4.4.3.3.0.<br>4.4.4.4.0. | 4.4.4.4.4.<br>0.0.0.0.0. | 86 ,, | 3 doses of 0·9 grm. of neosalvarsan intravenously. |
| 91 (p. 73) | 4.4.3.0.0.<br>4.4.4.1.0. | 3.2.1.0.0.<br>1.0.0.0.0. | 27 ,, | 2 doses of 0·6 grm. of salvarsan intravenously. |
| 94 | 1.0.0.0.0.<br>4.4.4.3.0. | 1.0.0.0.0.<br>0.0.0.0.0. | 25 ,, | 3 doses of 0·9 grm. of neosalvarsan intravenously. |
| 106 | 4.4.4.4.4.<br>4.4.0.0.0. | 0.0.0.0.0.<br>0.0.0.0.0. | 24 ,, | 2 doses of 0·6 grm. of salvarsan intravenously. |
| 120 (p. 89) | 4.2.0.0.0.<br>4.3.2.0.0. | 0.0.0.0.0.<br>0.0.0.0.0. | 35 ,, | 1 dose of 0·6 grm. of salvarsan intravenously. |
| 134 (p. 70) | 4.4.4.4.0.<br>4.4.4.4.4. | 2.0.0.0.0.<br>0.0.0.0.0. | 109 ,, | 1 dose of 0·6 grm. of salvarsan and 2 doses of 0·9 grm. of neosalvarsan intravenously. |
| 146 (p. 67) | 4.4.4.4.4.<br>4.4.4.4.2. | 4.4.1.0.0.<br>4.1.0.0.0. | 31 ,, | 3 doses of 0·9 grm. of neosalvarsan intravenously. |
| 147 (p. 22) | 0.0.0.0.0.<br>4.4.1.0.0. | 0.0.0.0.0.<br>0.0.0.0.0. | 30 ,, | 3 doses of 0·9 grm. of neosalvarsan intravenously. |
| 170 | 4.4.4.4.4.<br>4.4.0.0.0. | 4.4.4.0.0.<br>0.0.0.0.0. | 39 ,, | 3 doses of 0·9 grm. of neosalvarsan intravenously. |
| 244 | 4.4.4.3.0.<br>4.4.4.0.0. | 4.4.1.0.0.<br>0.0.0.0.0. | 25 ,, | 3 doses of 0·9 grm. of neosalvarsan intravenously. |
| 262 (p. 62) | 4.4.4.4.4.<br>4.4.4.4.0. | 4.4.4.0.0.<br>0.0.0.0.0. | 17 ,, | 3 doses of 0·9 grm. of neosalvarsan intravenously. |
| 309 (p. 32) | 4.-.-.-.-.<br>4.4.4.0.0. | 0.0.0.0.0.<br>2.0.0.0.0. | 13 ,, | 2 doses of 0·9 grm. of neosalvarsan intravenously and 8 injections of mercury cream into the buttock. |

* He had previously received 36 inunctions with mercurial ointment.

In the majority of cases the length of time between the two examinations is of little value except as indicating that the reaction became negative in the cerebrospinal fluid within a given number of weeks; we have no evidence that it had not become negative before the date of the second examination given on Table C. But on the whole we can say that the cerebrospinal fluid, though at first strongly positive, usually becomes negative in about six months; within a year all but one of the cases on Table C were completely negative in the cerebrospinal fluid.

The coincident amount of improvement shown by the patient depends entirely on the extent to which his signs and symptoms are, or are not, due to secondary changes in the central nervous system. If hæmorrhage has occurred into the spinal cord, as a consequence of rupture of a vessel weakened by endarteritis syphilitica, the patient will not show improvement coincident with the change for the better in his cerebrospinal fluid. Similarly, if some vascular blocking or local anæmia has led to secondary degeneration in one or more nerve-tracts it is obvious that the consequences of this degeneration will remain and the patient will continue, as before, to be spastic or ataxic. Thus it is of urgent importance to treat the patient early; for meningo-vascular syphilis is singularly amenable to treatment, and the permanent ill-effects due to this form of the disease are mainly due to secondary changes.

## Chapter V.—Syphilis Centralis.

Fournier's conception of "parasyphilis" was a disease which had syphilis for a necessary antecedent, though not in itself a manifestation of the specific virus; he based this view on the insusceptibility of such patients to anti-syphilitic treatment.

Now that we no longer agree with the first part of Fournier's definition but look upon all "parasyphilitic" manifestations as directly due to the activity of the *Spirochæta pallida*, we are obliged to ask ourselves why are diseases such as dementia paralytica and tabes dorsalis so little amenable to anti-syphilitic treatment? For, on the whole, cerebrospinal syphilis responds in a remarkable manner to mercury or salvarsan.

The answer has been given by Fildes and McIntosh [3], who showed that, as usually administered, the arsenical compounds, such as salvarsan and neosalvarsan, do not enter the structure of the central

nervous system in any effective quantity. Hence if the focus of disease lies in the substance of the central nervous system its activity will not be checked by drugs circulating in the blood-stream.

Fournier depended for his generalization on the fact that symptoms and signs in "parasyphilis" were but little influenced by treatment; we can add evidence in the same direction gathered from the behaviour of the Wassermann reaction in the cerebrospinal fluid. For in cases of meningo-vascular syphilis the reaction in the cerebrospinal fluid, if positive, can rapidly be rendered negative by treatment, whilst in "parasyphilis" it is little, if at all, affected.

But apart from this difficulty in reaching the focus of disease by means of such drugs there is another reason why many patients with tabes dorsalis and allied conditions do not respond to treatment. We believe that the neuroglia and essential tissues of the central nervous system have become hypersensitive in consequence of the previous activity of the *Spirochæta pallida*. Tracts of fibres, groups of cells and the neuroglia supporting them have been so highly sensitized that they now react with greater vehemence and to a smaller dose of the virus. Consequently tracts and nuclei degenerate whilst the neuroglia proliferates, and destruction of the nervous system may greatly exceed in extent the actual focus of fresh infective activity. In a case of tabes dorsalis destruction may run to an end in one or more tracts or nuclei and leave the patient in a quiescent stage of the disease with all the signs of gross degenerative changes in the central nervous system. Thus optic atrophy, when it once begins, invariably ends in blindness, but the disease may then make no further advance for many years; in the same way a man may be left with a grave ataxia which does not increase, for the disease has become completely quiescent, at any rate for a time.

Not only does the disease cease to advance but the Wassermann reaction in the cerebrospinal fluid may become negative and even a provocative injection of neosalvarsan may be unable to render it positive. In such patients the excess of cells, associated with the acute stage, may also disappear and the cerebrospinal fluid may not differ from that of a normal person (No. 83, p. 102).

From the clinical aspect however these patients are none the less suffering from tabes dorsalis, for they may show all the classical signs of absent knee-jerks, Argyll-Robertson pupils and gross ataxy; and yet in this quiescent stage there is no disease to treat. The flame has burnt itself out and left dead ashes on its path. In every

case of syphilis centralis it is important to consider how far the conditions presented by the patient are due to progressive disease, or to what extent they are the consequence of the activity of a virus which has ceased, at any rate for a time, to cause destruction in that particular part of the central nervous system.

### [A] Clinical Varieties.

#### § 1.—*Dementia Paralytica.*

Much of the confusion which has arisen with regard to the susceptibility of this disease to treatment and the behaviour of the Wassermann reaction in the cerebrospinal fluid springs from the notorious difficulty in making a differential diagnosis by clinical examination alone. There is not a symptom or a sign in dementia paralytica which cannot be present in a case of subacute meningo-vascular syphilis.

But the effect of treatment with anti-syphilitic remedies, especially the arsenical compounds, differs so greatly in the two conditions that the prognosis is fundamentally different. It is consequently impossible to class them together clinically, although in many cases they are indistinguishable at the bedside on the first examination. But by long continued observation and by watching the effect of treatment, not only on the patient but also on the Wassermann reaction in the cerebrospinal fluid, it is possible in many cases to separate these two conditions of such different prognostic import.

Compare the two following cases with one another:—

A woman of 39 (Case 120) was admitted to the London Hospital on June 28, 1912. She was walking along the road when she met a drunken woman whom she did not like; she became angry and excited and lost her speech. She was unable to move and was taken home in a cart. Next day, when admitted to the hospital, her memory was bad, her speech slurred and thick, but she was not aphasic or apraxic.

There was much tremor and unsteadiness of the left hand when the arm was extended; the right upper extremity was distinctly paretic and there was some diminution of power in the right lower limb; the left leg seemed to be unaffected. Both knee-jerks were brisk, but both plantar reflexes gave a flexor response and there was no ankle-clonus. The abdominal reflexes were obtained. The pupils were irregular, at times oval vertically, at times horizontally; they reacted to light, but the reaction was not maintained and they

fell into obvious oscillation. The reaction to accommodation was good. There was no ptosis, ocular paralysis, nystagmus or other abnormality within the territory of the cranial nerves except that the face was flattened, especially on the right side. The fundi were normal, and the sphincters unaffected.

Mentally she was dull, confused, worried. She thought "all was wrong at home," had other vague delusions, and could not sleep.

The Wassermann reaction was $\frac{\text{serum } 4.2.0.0.0.}{\text{cs.f. } 4.3.2.0.0.}$ and everything seemed to point to the diagnosis of dementia paralytica. But she was given injections of salvarsan and potassium iodide in considerable doses and an extraordinary change for the better rapidly occurred. By March, 1913, memory, attention and general intelligence had greatly improved and speech was no longer affected. Moreover the Wassermann reaction had become completely negative $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ This improvement has been maintained: in May, 1914, she no longer showed any nervous manifestations and had returned to her occupation. The Wassermann reaction was still negative in both serum and cerebrospinal fluid.

Here was a case which during the first period of clinical observation could not have been distinguished from one of dementia paralytica. Had she been sent to an Asylum there is little doubt she would have steadily degenerated and have been classed as an obvious instance of "general paralysis." After death no close microscopical examination would have been made in so commonplace a case and she would have swelled the list of those dying from that disease.

*A Case indistinguishable from one of "General Paralysis" where, under Treatment, both the Patient Recovered and the Wassermann Reaction became Negative in the Cerebrospinal Fluid.*

*Case* 120.—A. P., female, married; born 1874. In 1893, at the age of 19, she married her first husband, who died of "drink" four years later; to him she bore two children, one born in 1894, who died as a baby of "bronchitis," and a second born in 1896, who survived and is healthy. Shortly after marriage she suffered from a series of bad throats and her hair fell out.

In 1898 she married her second husband, and by him she has had (1) a child born in 1899 who died of "wasting," (2) a girl born in 1901, (3) a girl born in 1903, (4) a girl born in 1906, (5) a girl born in 1908; these pregnancies were followed by three miscarriages. The children born in 1901 and in 1903 give a positive Wassermann reaction in the blood, the child born in 1906 a negative reaction. The second husband also gives a positive reaction in the serum.

Four weeks before her admission on June 28, 1912, this patient miscarried. After the miscarriage she "never seemed well," and on June 27, 1912, she had a seizure, followed by loss of speech and paresis of the right hand.

On admission on June 28, 1912, she was muddled, inattentive and worried. She complained repeatedly that "everything was wrong at home," when in fact this was not the case. She was subject to causeless attacks of crying. Her memory was very defective. She only spoke when addressed, but her answers to questions were logical and to the point. Her speech was dysarthric, syllables were frequently slurred and badly pronounced. She did not complain of headache and was not subject to attacks of vomiting. Vision was unaffected. The vessels of the fundi were tortuous, but the edges of the optic discs were sharply defined. Hearing, smell and taste were unaffected.

The left eyelid drooped slightly but ocular movements were well carried out. The pupils were unequal in size, irregular in outline and only reacted sluggishly to light with the development of hippus; they reacted well to accommodation. Both sides of the face were flattened and there was definite paresis of the upper and lower halves on the right side. The tongue was very tremulous and on protrusion deviated to the right. The movements of the palate and larynx were unaffected.

Both hands were extremely tremulous. The right arm was paretic and the grasp of the right hand was feeble. The alignment of the fingers of the left hand was bad. No difference could be discovered between the muscular tone of the two upper extremities. There was some paresis of the right lower limb which cleared up rapidly after admission.

As far as could be determined there was no sensory loss.

The knee-jerks were clonic, the ankle-jerks were extremely brisk, but ankle-clonus could not be obtained. The wrist- and elbow-jerks were exaggerated. The abdominal reflexes on both sides were obtained. On the right side the plantar reflex gave a doubtfully extensor response, whilst on the left it was definitely flexor.

The sphincters and the movements of the spine were completely unaffected.

The urine contained albumen, and some granular casts were present. The vessels were thickened and tortuous and the left ventricle was enlarged. The blood-pressure in the brachial artery was 215 mm. The lungs were emphysematous. No abnormal physical signs were discovered in the abdomen.

On July 3, 1912, the Wassermann reaction was $\frac{\text{serum } 4.2.0.0.0.}{\text{cs.f. } 4.3.2.0.0.}$

She was given 0·6 grm. of salvarsan on July 6, 1912.

Eight months later, on March 5, 1913, the reaction was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells numbered less than 1 per cubic millimetre.

On March 7, 1913, she was given 0·9 grm. of neosalvarsan.

Since this treatment the serum has been tested on June 25, 1913, and on November 22, 1913, and on both occasions reacted negatively. On April 30, 1914, the Wassermann reaction was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and the cells again numbered less than 1 per cubic millimetre.

In May, 1914, both pupils reacted to light, though somewhat sluggishly and with a tendency to hippus. The face was still a little flattened on the right side, but there were no other abnormal signs in the territory of the cranial nerves. The reflexes were as before, but motion had greatly improved and no difference in power could be discovered between the two hands. She could now cut out dresses and fulfil all her domestic duties.

The brachial blood pressure still measured about 200 mm. and albumen was still present in the urine.

Compare the case of this woman with the following characteristic instance of dementia paralytica (No. 32). At first sight the likeness between the two is astonishing, but they differed in the consequences of treatment and the behaviour of the Wassermann reaction in the cerebrospinal fluid.

The patient was a man of 40, who, for about sixteen months before admission to the London Hospital, had complained of double vision and failure of sight in the right eye. He had been troubled for some time with shooting pains in the right leg, and, later on, in the right half of the trunk, associated more recently with weakness of the right arm and leg.

He was unusually well educated and intellectual, but his memory had become defective and he had lost the power of concentrating on his work. He was irrational, his attention was easily diverted, and he had lost his business instinct.

Speech was slurred, with indistinct articulation and a tendency to miss out syllables. The right hand was weak and tremulous and power was diminished in the right leg. There seemed to be some inco-ordination of the right upper extremity. His knee-jerks could be obtained but the ankle-jerks were abolished. Both the plantar and the abdominal reflexes responded normally. The right pupil was irregular in shape and larger than the left; both reacted badly to light, but readily to accommodation. The right external rectus and inferior oblique were weak, and diplopia was present when he moved his eyes to the right. The face was expressionless and flattened and the tongue was tremulous.

The Wassermann reaction was $\frac{\text{serum } 4.4.4.2.1.}{\text{cs.f. } 4.4.4.3.2.}$

He received two doses of 0·6 grm. of salvarsan, but grew steadily worse, and fourteen months later was an even more obvious case of dementia. He was loquacious and did not finish his sentences. He could not answer even simple questions because his attention wandered. He seemed to have no recollection of anything that had

happened during his last stay in the Hospital, and his memory was extremely bad.

His speech was profoundly slurred, and syllables and whole words were missed out. Gait was very unsteady and the movements of the upper extremities clumsy and inco-ordinate. There was no paralysis and the difference between the extremities on the two sides had disappeared. Both knee-jerks were obtained with difficulty; the right plantar reflex was usually extensor, whilst the left gave a flexor response. The pupils still reacted sluggishly to light, but the right was larger than the left and both were in shape irregularly oval. Lips and tongue were extremely tremulous. The sphincters were now affected and he suffered from overflow incontinence of urine.

The Wassermann reaction was $\frac{\text{serum } 4.4.4.4.0.}{\text{cs.f.} \quad 4.4.4.2.0.}$ almost identical with that obtained fourteen months before. Further injections of neo-salvarsan failed to check his downward course.

*A Case of Dementia Paralytica where the Positive Wassermann Reaction in the Cerebrospinal Fluid remained almost unaltered Fourteen months after Treatment.*

*Case* 32.—J. C., male, married, tailor: born 1872. In 1893, at the age of 21, when serving in the Russian Army, this patient caught "gonorrhœa" and suffered from a "running" which was not followed by any rash, sore throat, or other manifestation of secondary syphilis. He was treated for a few weeks only, and until the time of his marriage enjoyed good health.

In March, 1910, he married; his wife had never been pregnant. Shortly after his marriage he began to suffer from attacks of shooting pains in the legs, and later from "curious sensations" in his head and double vision, accompanied by a failure of the sight of the right eye. In the course of the next year his memory became defective: he lost all sexual power and began to complain of a weakness of the right half of his body. At that time he became less capable in business, his writing lost character and he became grandiose in his ideas.

He first came under observation in June, 1912, when he was admitted to the London Hospital under the care of Dr. Robert Hutchison.

He was a well-educated Hebrew, who had spoken four languages. He was intelligent but irrational. He had lost all business instinct. He talked freely of grand schemes by which he was going to change the face of Nature and make untold sums of money. During conversation the magnitude of these ideas could be raised by increasing degrees. His memory for recent events was extremely bad. He complained immediately after a big meal that "he was being starved," and said that "he was totally unable to sleep and had not slept a wink" after a good night's rest. His attention was fleeting. He

had not suffered from seizures or attacks of vomiting. His speech was slurred and many syllables or words in a sentence were missed out; this defect in speech was equally noticeable in Yiddish and in English.

He complained of headache over the right frontal region, but the scalp was not tender on pressure. Hearing, smell, taste, and vision were unaffected and the optic discs and fundi were normal.

He complained of double vision whenever he looked far to the right. The right external rectus and right inferior oblique muscles were paretic; but on closure of the left eye the right eyeball was seen to move freely in all directions. The right pupil was wide and eccentric and its margins were irregular; the left was well centred and regular in outline; both reacted sluggishly to light and briskly to accommodation. The face was flattened and tremulous in movement. The tongue on protrusion came out straight and was held steadily. The movements of the jaws, palate, and larynx were normal.

His gait was unsteady, but Romberg's sign was not obtained. The right hand could not be used to carry out fine movements and the tremor was visible in his writing. The writing was illegible and often undecipherable because words and syllables were missed out. The grasp of the right hand was feeble. The power of the right leg was weaker than that of the left.

His answers to the tuning-fork, the compasses, the prick of a pin, and the hot and cold tubes and to the tests for recognition of posture and passive movement were more accurate and more ready on the left half of the body than on the right; but there was no complete loss of sensibility anywhere. The answers obtained when using cotton-wool as a stimulus were more accurate than those obtained with any other form of testing.

On the left side the knee-jerk was brisk but the right was obtained on reinforcement only. Ankle-jerks could not be obtained. The abdominal reflexes were brisk. On the left side wrist- and elbow-jerks were readily obtained, on the right side they were doubtful. Both plantar reflexes gave a flexor response.

The patient had experienced no difficulty in holding or passing water, and no gross signs of disease were discovered in the heart, vessels, lungs, abdomen or urine.

On June 5, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.2.1.}{\text{cs.f.} \quad 4.4.4.3.2.}$

On June 7, 1912, he was injected with 0·6 grm. of salvarsan and this dose was repeated on June 12. On June 18, 1912, without a word of explanation he walked out of the hospital, went to a shop and ordered four suits of dress clothes and half a dozen top-hats.

He was not seen again until August 15, 1913, when he had altered but little mentally. He was loquacious and started many sentences, but rarely finished any statement. His answers to simple questions were irrational and inconsequent; his wife volunteered the statement that in Yiddish his answers were also bad. He could not remember any details of his previous admission to Hospital and denied that he had ever been an in-patient anywhere before.

Between June, 1912, and August, 1913, he had suffered from no seizures or attacks of vomiting. His speech was not much worse than on the previous admission. Vision was good and the optic discs and fundi appeared normal. The eye-movements were still defective, the face was flattened and the lips and tongue extremely tremulous. The movements of the hands were clumsy and the head and trunk took part in every volitional movement of the hands.

Both knee-jerks were sluggish, but could be elicited on reinforcement. The ankle-jerks were absent. The plantar reflexes either gave no responses or a sluggish extension. The jaw-jerk was much exaggerated.

Occasionally he wetted himself by day, and by night passed his water into the bed. Since his previous admission he had not been able to produce an erection.

On August 20, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.0.}{\text{cs.f. } 4.4.4.2.0.}$ and the cells numbered 24 per cubic millimetre.

The majority of patients with dementia paralytica, seen in the practice of a General Hospital in this country, approximate more to the type of tabo-paresis. The dementia usually causes loss of memory and aptitude for work with no exaltation or delusions; for any patient with acute mental symptoms finds his way rapidly into an Asylum by way of the Workhouse Infirmary, and does not pass through the hands of the neurologist.

Thus the cases of dementia paralytica used in this research are not a fair sample of the population, but are biassed in one direction in consequence of that complete divorce between neurology and psychiatry which unhappily obtains in this country. Although many of our patients ultimately entered an Asylum, they came to the Hospital not for mental symptoms but for seizures, loss of memory, or inability to work. They usually showed some affection of speech, tremor of the hands, face, and tongue, Argyll-Robertson pupils, and not infrequently absent knee-jerks with or without ataxy.

The following case (No. 200) is a good example of this condition. He was a man of 29, who was sent to us from the Rockefeller Institute, New York, for intensive treatment. At first the signs were those of tabes dorsalis, associated with tremor of the face and tongue and obvious mental instability. His general intelligence was not, however, greatly diminished. The Wassermann reaction was completely positive in the cerebrospinal fluid, and has remained so up to the present time in spite of intensive treatment with neosalvarsan intravenously and with serum injected into the lumbar sac after the method of Swift and Ellis [21]. At the same time his symptoms have become much

aggravated, and he is now grandiose and exalted; his speech is profoundly affected, and the tremors have greatly increased.

*A Case of Tabo-paresis with a completely Positive Wassermann Reaction in the Cerebrospinal Fluid; this remained Unaltered in Strength in spite of much Treatment and the Patient grew steadily worse.*

*Case* 200.—S. D., male, single, accountant; born 1883. This patient contracted syphilis in 1900, at the age of 17: he suffered from a chancre only and was treated with mercury and iodides by the mouth for eighteen months; no secondary manifestations of syphilis followed.

In the summer of 1911, he lost sexual desire, due, as he thought, to abuse of alcohol. In January, 1912, his left foot "became dead," and he then found that he could no longer hurry or jump and that he was unsteady when walking in the dark. About December, 1912, he began to suffer from pains in the legs, and for these he attended Dr. Arthur Ellis, of the Rockefeller Institute, New York, who sent him to us for "intensive treatment with salvarsan."

He first came under our observation in May, 1913, and was admitted to the London Hospital on June 8, 1913.

At this time he was irrational, emotional and subject to attacks of crying. Memory and attention were fair and his speech little affected. He could reason, but doubted his own conclusions. He had never suffered from headache or attacks of nausea or vomiting.

Vision was unimpaired, the optic discs were healthy, and hearing, smell, and taste unaffected.

The right pupil was larger than the left; both responded sluggishly to light and the contraction was ill-sustained, but they reacted briskly to accommodation. The movements of the eyes, face, palate, and larynx were normal, but the tongue, though protruded straight, could not be held steadily and was intensely tremulous.

His gait was ataxic and Romberg's sign was present. The alignment of his fingers was bad, and on closing the eyes the outstretched hands fell away from the position in which he intended to hold them. The muscles of the extremities were well developed and showed no loss of tone.

He complained of shooting pains in the legs and of a constant "gnawing ache in his knees." In the lower extremities there was much loss of the power of appreciating posture and passive movement, the compasses and the vibrations of the tuning-fork. He recognized the shape, size, form and consistence of objects placed in his hands with difficulty. To tests with cotton-wool, with the prick of a pin and with the hot and cold tubes no disturbance of sensibility could be discovered.

Neither knee-jerk could be obtained even on reinforcement, and the ankle-jerks were abolished. The wrist- and elbow-jerks were normal and the abdominal reflexes brisk, but no plantar reflexes could be obtained on stimulation either of the soles or of the front of the ankles.

He experienced no difficulty either in holding or in passing water, but for two years he had been unable to produce an erection of the penis.

No abnormal signs were discovered in the heart, lungs, or abdomen, and the urine contained neither albumen nor sugar.

On June 11, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.3.}{\text{cs.f. } 4.4.4.4.4.}$ and the cells numbered 22 per cubic millimetre.

He was injected intravenously with doses of 0·9 grm. of neosalvarsan on June 12 and June 21, 1913; after each injection he complained of much headache, nausea, and vomiting, and on June 22 his temperature rose to 101° F. (38·3° C.). The attack of vomiting after the first injection lasted sixty hours and during this time morphia only, of the many drugs administered, had any effect either in quieting the patient or in stopping the attack of vomiting. On June 23 he developed a temporary state of mental confusion in which he constantly repeated commands and statements such as "thanks very much," and laughed immoderately: yet when his attention was gained his conversation was rational and his ideas consecutive. This attack lasted some twenty-four hours and during this time he vomited six times. On June 27 he seemed to have returned to the state in which he was admitted: 0·9 grm. of neosalvarsan were administered; no abnormal reaction followed this injection.

After this he was discharged and treated with potassium iodide from July 1 until September 29. He was then injected intravenously on:—

| | | | | | |
|---|---|---|---|---|---|
| September | 29 | with | 0·2 | grm. | of neosalvarsan. |
| October | 3 | „ | 0·3 | „ | „ |
| October | 7 | „ | 0·3 | „ | „ |
| October | 10 | „ | 0·3 | „ | „ |

On January 14, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.4.4.}$ and the cells numbered 3 per cubic millimetre.

In January, 1914, his mental condition was worse than it had been in the previous June. He was self-conscious, restless, excitable, and exalted, boasting freely of his great abilities. He was intelligent, argumentative and self-opinionated, but at the same time obsequious and deferential. He said that he could walk miles and was the equal of any man living in fighting, although his gait was ataxic and his power of walking poor. He talked freely to sister and nurse about sexual matters. His memory was very defective and his power of attention poor. Sleep was disturbed but was not accompanied by dreams or nightmares.

His speech was extremely jerky and his words badly enunciated, whilst his writing was tremulous, unsteady, and hardly decipherable.

His lips and tongue were intensely tremulous and in every minor action of his hands his whole body moved. Otherwise no fresh manifestations could be discovered within the territory of the cranial nerves.

He stood stiffly at attention and walked with a stamping, ataxic gait, waiving his arms and swaggering with exaltation at his prowess. The left leg was more ataxic than the right, and the upper extremities clumsy and incoordinate.

He no longer complained of pains and on this account was intensely pleased,

and talked to everybody he met about the wonderful improvement he had made under the new therapeutic method. With these exceptions his physical signs were unchanged.

On January 16, 1914, he was again injected with 0·9 grm. of neosalvarsan, and on January 22, February 10, 17, and 22, he was given intrathecally doses of 10 c.c. of his own "salvarsanized serum," collected sixty minutes after the injection of January 16.

Since this treatment no improvement, either in mental or physical state, has occurred, and he is now (July, 1914) a characteristic example of tabo-paresis with exaltation and delusions of grandeur.

On July 8, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.}{\text{cs.f.} \quad 4.4.4.4.}$ and the cells numbered 18 per cubic millimetre.

We have collected in the course of this research 22 cases of dementia paralytica and tabo-paresis, including three instances of the juvenile form of the disease. In every case, as will be seen from Table D, the cerebrospinal fluid gave a strong positive reaction. Our results, as far as they go, agree exactly with the original statement of Plaut and with Mott's observations on Asylum patients with dementia paralytica. The more carefully patients are differentiated by clinical observation and by watching the results of treatment on the cerebro-spinal fluid, the greater will be the percentage of positive reactions obtained in cases of dementia paralytica; we have not yet seen an instance of a negative Wassermann reaction in the cerebrospinal fluid.

Thus, in conclusion, we believe that cases of syphilis meningo-vascularis cerebralis may be distinguishable from dementia paralytica solely by the fact that the cerebrospinal fluid, from the first, gives a negative reaction. But if, as is so commonly the case, some intraspinal complication is present, the cerebrospinal fluid in both diseases may be equally positive; they are then not infrequently indistinguishable from one another, except by watching the effect of treatment. For in dementia paralytica the symptoms and signs do not improve to any considerable extent, and the positive Wassermann reaction is not materially reduced in the cerebrospinal fluid, even by the most energetic treatment with salvarsan and neosalvarsan.

This we attribute to the situation of the lesions in syphilis centralis, of which dementia paralytica is the cerebral form; the focus of infection lies deep in the nervous system in parts not in direct connexion with the blood-stream. Consequently drugs circulating in the blood cannot materially affect the lesion in central syphilis of the nervous system.

TABLE D.—THE INCIDENCE OF THE WASSERMANN REACTION IN DEMENTIA PARALYTICA AND TABO-PARESIS.

| No. of case | Result on first examination | No. of case | Result on first examination |
|---|---|---|---|
| 20 (Autopsy) | serum 4.4.4.3.1.<br>cs.f. 4.4.4.4.1. | 119 (Autopsy) | serum 4.4.4.4.4.<br>cs.f. 4.4.4.4.4. |
| 32 (p. 92) | 4.4.4.2.1.<br>4.4.4.3.2. | 152 | 4.4.4.3.1.<br>4.4.4.0.0. |
| 33 | 4.4.4.4.4.<br>4.4.4.0.0. | 165 | 4.4.3.2.1.<br>4.4.4.4.0. |
| 80 | 4.4.4.3.2.<br>4.4.4.4.4. | 169 | 4.4.4.4.4.<br>4.4.4.4.4. |
| 82 | 4.4.3.1.0.<br>4.4.4.4.1. | 200 (p. 95) | 4.4.4.4.3.<br>4.4.4.4.4. |
| 84 (Autopsy) | 4.4.4.4.4.<br>4.4.4.4.4. | 214 | 4.4.4.4.1.<br>4.4.4.4.4. |
| 90 (Autopsy) | 4.4.4.4.2.<br>4.4.4.4.0. | 230 (Autopsy) | 4.4.4.4.4.<br>4.4.4.4.4. |
| 95 | 4.4.4.3.2.<br>4.4.4.3.2. | 285 | 4.4.4.4.2.<br>4.4.4.4.2. |
| 96 (Autopsy) | 4.4.4.4.3.<br>4.4.4.4.2. | 304 | 4.4.4.4.4.<br>4.4.4.4.0. |
| 108 | 4.4.4.4.0.<br>4.4.4.4.3. | | |

JUVENILE.

| No. of case | Result on first examination | No. of case | Result on first examination |
|---|---|---|---|
| 16 (Autopsy) | serum 4.4.4.4.4.<br>cs.f. 4.4.4.4.4. | 197 | serum 4.4.4.4.4.<br>cs.f. 4.4.4.2.0. |
| 109 | 4.4.4.4.4.<br>4.4.4.4.3. | | |

## § 2.—*Tabes Dorsalis.*

Year by year the line, once so firmly drawn between tabes dorsalis and dementia paralytica, grew fainter as the identity of the pathological process underlying the two diseases was recognized. Cases were described which started as tabes dorsalis and ended in dementia paralytica, and destruction of the posterior columns of the spinal cord was often found *post mortem* in characteristic instances of "general

paralysis." With the invention of "taboparesis" as a diagnostic expression, the boundaries between the two diseases fell once for all; it was recognized that they were not two separate pathological states, but manifestations of the same process attacking different parts of the central nervous system.

In the same way the conception of tabes dorsalis had to be widened to take in atrophy of the muscles and occasionally even lateral sclerosis; primary optic atrophy, associated with normal reflexes, has also been included amongst the forms of tabes dorsalis. (Nonne [13], p. 174.) Here also no natural boundaries can be erected between these various "parasyphilitic" states; all of them are manifestations of the same pathological process working on different parts of the nervous system.

All attempts to maintain tabes dorsalis as a separate disease must, therefore, be given up and the term confined to a set of signs and symptoms depending mainly on degeneration of the posterior columns of the spinal cord consequent on syphilitic infection. Thus the word taboparesis may be used to describe a case with definite signs of affection of the posterior columns of the cord which at the same time or subsequently showed loss of memory, seizures, altered speech, or paresis, pointing to a corresponding form of cerebral affection. In the same way it is better to speak of amyotrophy and tabes dorsalis, rather than of "amyotrophic tabes"; for the two conditions are caused by the same process acting on different structures, and neither is in the strict sense of the word a disease.

In this section we shall deal solely with cases in which the principal signs pointed to affections of the posterior columns of the spinal cord. "Taboparesis" has been included with dementia paralytica; amyotrophy, primary optic atrophy, and epilepsy, due to syphilis centralis, will be dealt with in subsequent sections.

The signs upon which we shall depend to show the affection of the posterior columns are absence of the ankle-jerks and knee-jerks accompanied by certain changes in sensation with or without some ataxy of the upper or lower extremities. These changes in sensation consist for the most part in diminished appreciation of the vibrations of a tuning-fork (C. = 128), inability to recognize the position into which the segments of the limb have been placed passively, and failure to appreciate the compass-test even when the points are separated to extreme distances, such as 15 cm.

Such then are the signs upon which we have relied in constructing the following table. All cases of taboparesis have been included under

dementia paralytica, and the other varieties of syphilis centralis ("parasyphilis") have been relegated to their appropriate sections. For tabes dorsalis can no longer be looked upon as a disease, but is one variety only of central syphilis of the spinal cord.

TABLE E.—THE INCIDENCE OF THE WASSERMANN REACTION IN TABES DORSALIS.

| No. of case | Result on first examination | No. of case | Result on first examination |
|---|---|---|---|
| 11 | serum 4.4.4.4.4.<br>cs.f. 4.4. - - - | 132 | serum 4.4.0.0.0.<br>cs.f. 4.4.4.0.0. |
| 23 | 4.4.4.4.4.<br>4.3.0.0.0. | 142 | 4.4.4.0.0.<br>4.4.4.0.0. |
| 27 | 4.4.4.3.0.<br>3.1.0.0.0. | 143 | 4.4.4.4.0.<br>4.4.1.0.0. |
| 30 | 4.1.0.0.0.<br>4.4.4.4.0. | 144 (p. 104) | 0.0.0.0.0.<br>0.0.0.0.0. |
| 37 (p. 107) | 4.4.2.0.0.<br>4.4.3.1.0. | 145 | 4.3.2.0.0.<br>4.4.3.3.0. |
| 46 | 4.4.4.4.3.<br>3.0.0.0.0. | 150 | 4.4.4.4.2.<br>4.4.3.0.0. |
| 50 | 4.4.4.4.1.<br>0.0.0.0.0. | 199 (p. 118) | 4.4.4.4.0.<br>4.4.4.4.0. |
| 55 | 4.3.1.0.0.<br>4.4.3.1.0. | 224 (p. 119) | 4.4.4.4.4.<br>4.4.4.0.0. |
| 56 | 4.4.4.4.1.<br>4.4.4.4.1. | 234 | 4.4.4.4.4.<br>4.4.3.1.0. |
| 58 | 4.3.1.0.0.<br>4.4.4.1.0. | 257 | 4.4.4.4.0.<br>4.4.0.0.0. |
| 67 | 4.3.2.0.0.<br>4.4.4.0.0. | 258 | 4.4.4.4.0.<br>4.4.4.0.0. |
| 70 | 4.4.4.2.0.<br>4.3.0.0.0. | 278 | 4.4.4.0.0.<br>4.4.4.0.0. |
| 83 (p. 102) | 2.0.0.0.0.<br>0.0.0.0.0. | 294 | 4.4.4.4.0.<br>4.4.4.4.0. |
| 112 | 4.4.4.4.4.<br>4.4.4.4.4. | 295 | 4.4.4.4.0.<br>4.4.2.0.0. |
| 117 | 2.0.0.0.0.<br>4.4.4.4.1. | 300 | 4.4.4.4.4.<br>4.4.4.4.0. |
| 131* | 4.3.2.1.0.<br>4.4.4.3.1. | | |

* An account of this case was given in BRAIN, 1913, vol. xxxvi, p. 12.

With regard to the Wassermann reaction in tabes dorsalis, we have little to say that is not in complete agreement with the statements of other observers. Out of thirty-one cases twenty-eight were positive in cerebrospinal fluid, a result in general harmony with that of Nonne and Mott.

Two of the cases (No. 83 and No. 144) which gave a negative reaction in the cerebrospinal fluid are extremely instructive.

No. 83 was a man aged 55, who was infected at the age of 27. Some five or six years later he began to suffer from shooting pains in his legs, and slowly became ataxic. At the age of 42 he was an out-patient at the London Hospital with obvious tabes dorsalis, but for many years before this he had suffered from occasional retention of urine.

In April 1913, at the time our first observations were made, he was admitted because he had suddenly developed a Charcot knee.

He was profoundly ataxic, and fell when his eyes were closed; the muscles of legs and thighs were grossly hypotonic. All power of recognizing vibration, posture, and passive movement was lost in both lower extremities, and there was much delay, though no absolute loss, in the appreciation of pain, heat, and cold. Knee- and ankle-jerks were abolished. Neither pupil responded to light, and the right external rectus acted feebly. The left knee was disorganized, and much distended with fluid. Retention of urine with overflow was present, the bladder reaching to the umbilicus on admission.

Here was a straightforward case of tabes dorsalis, but the Wassermann reaction was $\frac{\text{serum } 2.0.0.0.0.}{\text{cs.f.} \quad 0.0.0.0.0.}$ and the cells in the cerebrospinal fluid were not in excess of normal. He was given two injections of 0·9 grm. of neosalvarsan, but no provocative reaction was produced. Evidently we were dealing with a case where the disease had died out, leaving behind it destruction of the posterior columns of the spinal cord.

Compare with this patient No. 144, who also yielded a negative reaction in the cerebrospinal fluid. He was a man aged 42, who was infected with syphilis at the age of 30; this was followed by a chancre and rash, but he was treated for one month only.

In April, 1908, he began to notice numbness of the legs with pains and dribbling of urine. He was then treated with mercury by the mouth, and probably with injections of salvarsan in Canada.

When admitted to the London Hospital in July, 1912, he was

intensely ataxic, and could not stand at all. All the muscles of the lower extremities, and to a less extent those of the arms, were hypotonic. Vibration was not appreciated anywhere below the level of the nipples, and recognition of posture and passive movement was lost in the legs, and gravely diminished in the arms. Sensation of pain, heat, and cold was delayed below the level of the groins, but was not completely lost. The knee-jerks and ankle-jerks were abolished and the wrist-jerks were obtained with difficulty. He suffered from true incontinence of urine, and at times had attacks of rectal tenesmus.

His Wassermann reaction was negative in the serum and cerebrospinal fluid. On July 18 he was given 0·6 grm. of neosalvarsan, and on July 24 and 25 the reaction was $\frac{\text{serum } 1.1.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$; on July 29 and 30 it was $\frac{\text{serum } 4.4.4.1.0.}{\text{cs.f. } 0.0.0.0.0.}$ The next day (August 1) he was given another injection of 0·9 grm. of neosalvarsan; and on August 7 the reaction was $\frac{\text{serum } 4.4.4.3.1.}{\text{cs.f. } 1.0.0.0.0.}$ By October 8 it had again become completely negative, $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and so it remained.

Here, then, is an instance where the disease was not active, but had not entirely burnt itself out; an injection of neosalvarsan could provoke a positive reaction in the serum, though not in the cerebrospinal fluid, which remained negative throughout, showing that in the central nervous system the activity of the pathological process was apparently at an end.

*A Case of Tabes Dorsalis where the Infection had apparently died out. Negative Wassermann Reaction in the Cerebrospinal Fluid.*

*Case* 83.—E. I., male, married, general dealer; born 1858. In 1885, at the age of 27, this patient contracted a chancre, which was followed by the development of a bubo in the right groin. He received treatment for four weeks only.

In 1890 he began to complain of shooting pains in the legs: these were soon followed by the development of ataxy and trouble with micturition.

In 1901 he attended as an out-patient at the London Hospital for incontinence of urine and "cystitis," and was diagnosed as a case of tabes dorsalis on the absence of his knee-jerks, the presence of lightning pains, ataxy and Argyll-Robertson pupils.

In the Autumn of 1912 a large painless swelling of the left knee appeared: in four days the swelling became so great that he was no longer able to walk.

He has attended at the London Hospital since December, 1912, and was admitted in April, 1913, when he showed all the signs of tabes dorsalis. His mental state was unaffected, and his speech natural. In the past he had been subject to attacks of vomiting, but not in recent years. The optic discs were pale, but the vessels were of normal size and there were no signs of optic atrophy. Vision, smell, taste and hearing were unaffected.

There was no ptosis. The right external rectus muscle acted weakly, otherwise the ocular movements were normal. The left pupil was larger than the right: both were excentric and neither reacted to light, but they reacted well to accommodation. The features were flattened, but there was no paresis of the face and the tongue on protrusion came out straight and was held steadily.

His gait was characteristically ataxic and Romberg's sign was present. The legs were gravely hypotonic, but the tone of the muscles of the arms was unaffected, and the alignment of the fingers was good.

He complained of occasional spontaneous shooting pains in the legs, which he stated were much less severe than they had been at the onset of the nervous manifestations. To tests on the legs and on the trunk below the level of the umbilicus with the hot and cold tubes, with the prick of a pin and painful pressure there was considerable delay before answers were obtained. He had completely lost all power of appreciating posture and passive movement and the vibrations of the tuning-fork on both legs. The weight, size, shape, form and consistence of objects placed in the hands were well recognized and there was no falling away of the outstretched hands on closure of the eyes. On the legs the light touch of cotton-wool was less affected than any other form of sensibility. To the dragged point of a pin and the pinching of the skin there was definite hyperalgesia over the distribution of the eleventh and twelfth thoracic nerve-roots.

Superficial bed-sores were present on the sacrum. The left knee showed all the characteristics of Charcot's disease, and was enormously swollen; it allowed great lateral displacement and an X-ray photograph showed much bony erosion and change.

The knee-jerks were abolished and the ankle-jerks could not be obtained. The wrist- and elbow-jerks and abdominal reflexes were natural, and both plantar reflexes gave flexor responses.

He had difficulty in passing his urine and on admission was suffering from overflow from a bladder distended to the umbilicus; he had no difficulty in controlling his motions even when soft. The spine was straight and moved naturally.

The cardiac sounds were clear and the lungs emphysematous. The blood-pressure on the right brachial artery was 120 mm. The urine was alkaline and contained much pus and albumen.

On April 9, 1913, the Wassermann reaction was $\frac{\text{serum } 2.0.0.0.0.}{\text{c.s.f.} \quad 0.0.0.0.0.}$ and the cells numbered 1 per cubic millimetre.

On April 10, 1913, he was injected with 0·9 grm. of neosalvarsan. To this injection no provocation of the Wassermann reaction occurred, for on April 21, 1913, it was still $\frac{\text{serum } 2.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$

Under rest in bed the swelling of the left knee diminished and on May 30, 1913, he was discharged wearing a long poroplastic splint, feeling "better than he had felt for years."

*A Case of Tabes Dorsalis with a Negative Wassermann Reaction in the Serum and Cerebrospinal Fluid. A "Provocative" Positive Reaction appeared in the Serum after Treatment, but not in the Cerebrospinal Fluid.*

*Case* 144.—A. S., male, single, shoemaker: born 1870. In 1900, at the age of 30, he contracted syphilis and suffered from a chancre, which was not followed by any rash or sore throat; he treated himself for four weeks with mercury.

In April, 1908, he began to be troubled with numbness in the legs, and about August of that year first experienced difficulty in walking. Shortly after the development of these symptoms he began to have difficulty in starting the act of micturition, and later suffered from incontinence of urine from overflow. About the same time he began to suffer from attacks of sharp shooting pains in the legs and a sense of fulness in the throat. From April, 1908, until July, 1909, the symptoms increased very rapidly, and in the latter month he was admitted to the Ottawa Hospital, where he received a course of inunctions with mercury. He remained an in-patient until November, 1909, but despite the mercurial treatment new symptoms continued to develop. In February, 1910, he was admitted to the Montreal Hospital and was treated with injections of salvarsan and also of mercury. Under this treatment the active progress of his symptoms subsided, and between July, 1910, and July, 1912, no fresh manifestations appeared.

He was admitted to the London Hospital in July, 1912, and remained an in-patient until December, 1912. His mental state was normal and his speech was unaffected. He was subject to irregular pyrexial attacks, in which the temperature rose to 100° F. (37·7° C.) without apparent cause. In these pyrexial attacks the rate of the pulse increased correspondingly from about 88 to 100 beats per minute. He complained of no headache. During the months of October, November, and December, 1912, he was subject to paroxysmal vomiting (gastric crises) lasting on each occasion one or two days. Whilst an in-patient he also suffered from attacks of rectal tenesmus (rectal crises) and occasional difficulty in swallowing.

Vision was unaffected. The optic discs were pale, the vessels of the fundus small, but there was no definite evidence of primary optic atrophy. Hearing, smell, and taste were unaffected.

The right external rectus muscle was completely paralysed and the patient suffered from a permanent squint. The pupils were small and their outlines were irregular; neither reacted to light, but both reacted to accommodation.

The face was flattened and expressionless. The movements of the tongue, palate, and larynx were unaffected.

The gait was intensely ataxic, and he could not stand at all with his eyes closed. The musculature of the lower extremities was poorly developed and the muscles themselves were hypotonic.

He complained of spontaneous grinding and shooting pains in the legs. There was grave loss of the sense of posture and passive movement in the hips, knees, ankles, toes, and considerable loss in the fingers, wrists, and elbows. Below the level of the nipples on both sides he could not appreciate the vibrations of a tuning-fork. The response to the prick of a pin, to painful pressure, to heat and cold in both legs was impaired and greatly delayed. Everywhere the appreciation of cotton-wool was less affected than any other form of sensibility.

The knee-jerks and ankle-jerks were abolished. The abdominal reflexes were readily obtained and the plantar reflexes on both sides gave brisk flexor responses. The jaw-jerk was natural.

He could not hold his water, and suffered either from incontinence of urine or precipitancy in micturition: he complained of attacks of rectal tenesmus, but at other times experienced no difficulty in controlling his motions.

The spine moved freely, but showed a general dorso-lumbar convexity.

His vessels were thickened and tortuous, but no abnormal signs were discovered in the heart, lungs, abdomen, or urine.

On July 10, 1912, the Wassermann reaction was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$ and on July 16, 1912 $\frac{\text{serum } -.-.-.-.-.}{\text{cs.f. } 0.0.0.0.0.}$

On July 18, 1912, he received 0·6 grm. of neosalvarsan and the reaction was tested on

July 18, $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } -.-.-.-.-.}$
July 20, $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } -.-.-.-.-.}$
July 22, $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } -.-.-.-.-.}$
July 24, $\frac{\text{serum } -.-.-.-.-.}{\text{cs.f. } 0.0.0.0.0.}$
July 25, $\frac{\text{serum } 1.1.0.0.0.}{\text{cs.f. } -.-.-.-.-.}$
July 29, $\frac{\text{serum } -.-.-.-.-.}{\text{cs.f. } 0.0.0.0.0.}$
July 30, $\frac{\text{serum } 4.4.4.1.0.}{\text{cs.f. } -.-.-.-.-.}$

It will be seen that a "provocative" reaction appeared in this case in the serum, but not in the cerebrospinal fluid, seven to twelve days after an injection of 0·6 grm. of neosalvarsan.

On August 1, he received another injection of 0·9 grm. of neosalvarsan, and the Wassermann reaction on August 7 was $\frac{\text{serum } 4.4.4.3.1.}{\text{cs.f. } 1.0.0.0.0.}$

On August 10 another injection of 0·9 grm. of neosalvarsan was given, and the reaction on October 8 was $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } 0.0.0.0.0.}$

On October 14 he received another dose of 0·6 grm. of neosalvarsan, and on October 23, 1912, the serum still reacted negatively $\frac{\text{serum } 0.0.0.0.0.}{\text{cs.f. } -.-.-.-.-.}$

Although the serological reactions altered in this manner under treatment no change occurred in the signs or symptoms of disease.

Now although many patients with tabes dorsalis may reach this stage, most of them come under observation at a time when the disease is active and both serum and cerebrospinal fluid are strongly positive. This reaction remains unaltered by anti-syphilitic treatment in tabes dorsalis, as in other forms of syphilis centralis, even although the treatment is carried out over periods amply sufficient to produce a profound change in cases of syphilis meningo-vascularis. But in the course of some years, if the patients survive the various intercurrent complications, a certain proportion tend to pass into a state of quiescence, in which they are left with signs of destruction of some portion of the nervous system, but no active disease. In this stage the Wassermann reaction may become negative in the cerebrospinal fluid.

The majority, however, of the patients with tabes dorsalis come under observation at a time when the disease is actively progressive, and correspond more closely with the following instance.

No. 37 was a man aged 41 who was infected at the age of 25 and treated with mercury off and on for the next ten years. He was admitted to the London Hospital in October, 1912. For many years he had suffered from shooting pains in the legs and in 1904 was discovered to have Argyll-Robertson pupils.

On admission his gait was ataxic and he fell when his eyes were closed. Ataxy was confined to the lower extremities, where there was considerable loss of appreciation of posture, passive movement and vibration. Sensibility to prick was gravely defective, and there was also some want of appreciation of heat and cold. Touch was unaffected. The pupils were irregular and reacted to accommodation but not to light. Knee-jerks and ankle-jerks were abolished. He suffered occasionally from difficulty in passing his water.

His Wassermann reaction on October 8, 1912, was $\frac{\text{serum } 4.4.2.0.0.}{\text{cs.f. } 4.4.3.1.0.}$

He was given repeated doses of 0·9 grm. of neosalvarsan, but on September 3, 1913, the reaction showed no material change and was serum 4.4.4.2.0.
cs.f. 4.4.2.0.0.

*A Case of Tabes Dorsalis with a Positive Wassermann Reaction in the Cerebro-spinal Fluid. No Material Change under Treatment.*

*Case* 37.—C. C., male, married, cycle agent; born 1871. This patient contracted syphilis in 1896, at the age of 25, and suffered from a chancre, recurrent sore throats, a rash on the chest and aching pains all over. He was treated with mercurial pills by the mouth from 1896 to 1898, and again at intervals during the years 1902 to 1912.

He married in 1891; his wife had one healthy child born in 1896 and no miscarriages.

About 1902 he began to suffer from a syphilitic affection of the tongue, which in the years 1902 to 1908 always yielded promptly to the administration of mercury, until in 1908 it became a typical leucoplakia.

In about 1904 nervous symptoms began with shooting pains in the legs and some degree of ataxia. He is known to have had Argyll-Robertson pupils and an affection of the bladder since 1906; since this time he had always experienced difficulty in obtaining an erection of the penis. Between 1908 and 1912 he believed that the "tabetic" symptoms had been stationary.

In the spring of 1912 an ulcer developed on the right side of his tongue and for this he was admitted on October 4, 1912, to the London Hospital.

On the right half of the tongue was a large epitheliomatous growth, 1½ in. by 1 in. (3·8 by 2·5 cm.), with a shallow ulcer on the outer margin, whilst the rest of the tongue showed a characteristic leucoplakia. No enlarged secondary glands were felt in the neck. The tongue was fairly freely movable, and on October 23, 1912, Mr. Hutchinson removed the right half and the glands of the submaxillary region, and ligatured the right lingual artery in the neck.

His vessels generally were thickened and tortuous; the aortic second sound was accentuated; the lungs showed moderate emphysema, but no abnormal physical signs were discovered in the abdomen or urine.

His mental state and memory were unaffected. Speech was natural, and he had never suffered from attacks of nausea or vomiting. He did not complain of any headache. Hearing, smell, taste and vision were unaffected, and the optic discs and fundi on both sides appeared natural.

Ptosis of the left upper eyelid was present. The left pupil was irregular in outline, oval in shape with the long axis vertical and reacted sluggishly to intense light; the right pupil was well centred and regular in outline but did not react even to the most intense illumination. Both pupils reacted well on accommodation and convergence. The ocular movements were unimpaired. The face moved symmetrically and its expression was normal. The tongue was protruded straight and held steadily. The movements of the palate and larynx were unaffected.

His gait was typically ataxic and Romberg's sign was obtained. There was no muscular wasting. The fingers could be brought into perfect alignment and there was no falling away of the hands on closing the eyes. The tone of the muscles of the legs was almost normal.

He complained of occasional attacks of lightning and grinding pains in the legs. There was considerable loss of the ability to recognize posture and passive movements in the legs, and an almost complete inability to appreciate the vibrations of the tuning-fork and the compass-points on both legs. Painful pressure, the prick of a pin, and the hot and cold tubes were recognized after a delay on both legs, and their recognition led to "drawing away" reflexes of large extent involving the whole of the limb stimulated.

The knee-jerks were completely abolished and ankle-jerks could not be obtained, whilst the plantar reflexes on both sides gave a flexor response. The abdominal reflexes were readily elicited.

The patient complained of precipitancy of micturition and occasional attacks of urinary retention with overflow.

On October 8, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.2.0.0.}{\text{cs.f.} \quad 4.4.3.1.0.}$

He was given 0·9 grm. of neosalvarsan, and before operation the ulcer of the tongue diminished in size. On November 3, 1912, after the operation, he was again injected with 0·9 grm. of neosalvarsan.

On May 4, 1913, he received another injection of 0·9 grm. of neosalvarsan.

On May 7, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.2.0.}{\text{cs.f.} \quad 4.4.2.0.0.}$ and the cells numbered 30 per cubic millimetre.

In May, 1913, he stated that since his first injection his general health had much improved, the lightning pains had ceased and were now replaced by bearable discomfort in the legs. At the same time the knee-jerks had reappeared so that the left was now readily obtained and the right could be obtained with reinforcement: the left ankle-jerk was present and the right was brisk. No changes had appeared, however, in the territory of the cranial nerves.

On May 8, 1913, he complained of a tender spot on the inner fold of the right buttock, and here a patch of herpetic vesicles was seen covering an area $\frac{1}{4}$ inch by $\frac{1}{4}$ inch (6 by 6 mm.).

Shortly after this date secondary malignant glands appeared on the right side of the neck. These were treated by further removal and later by X-rays. In July, 1913, the wound broke down and the surface of the skin around the wound ulcerated.

On September 3, 1913, the nervous signs were similar to those found in the previous May, and the Wassermann reaction was identical $\frac{\text{serum } 4.4.4.2.0.}{\text{cs.f.} \quad 4.4.2.0.0.}$

In December, 1913, he died of secondary carcinomatosis: and no *post-mortem* examination was allowed.

Thus we believe that, although neither the symptoms nor physical

signs of tabes dorsalis are materially affected by anti-syphilitic treatment the disease in many cases tends to become quiescent. The more nearly this stage is reached the weaker is the Wassermann reaction in the cerebrospinal fluid and the fewer cells does it contain. After a quiescent period, however, the disease may start again; some other structure such as the optic nerves may become affected and run on to complete degeneration.

Thus in tabes dorsalis the character of the Wassermann reaction in the cerebrospinal fluid depends on the state of the disease; if it is actively progressive the reaction will be highly positive and the cells excessive. But if the signs are only the results of a process which has come to an end permanently, or for a time, the reaction may be completely negative in the cerebrospinal fluid, even without anti-syphilitic treatment.

### § 3.—*Muscular Atrophy.*

We have already spoken of those cases of muscular atrophy due to syphilis, where the signs and symptoms are obviously caused by changes in the meninges and vessels. But, as many observers have pointed out, such an explanation does not fit every example of amyotrophy arising on a syphilitic basis, and fails especially in cases where muscular atrophy accompanies tabes dorsalis.

It will be well, therefore, to consider the various views that have been put forward with the hope that we may be able to suggest a solution which will result in greater certainty of diagnosis and prognosis.

In 1893 Raymond [20] brought forward some cases of muscular atrophy in one of which an autopsy was obtained. This revealed vascular and perivascular lesions leading to destruction of the anterior horn-cells. By some curious misapprehension Fournier ([4], p. 262) bases on these cases his view that uncomplicated muscular atrophy may occur in "parasyphilis." Léri [7], however, rightly uses Raymond's observations as a support to his view of the meningo-vascular origin of syphilitic amyotrophy.

Dejerine [1] in 1889 laid stress on the frequent occurrence of muscular atrophy in tabes dorsalis, and attributed it to peripheral neuritis; he was unable to find the degeneration of anterior horn-cells described by Raymond.

Léri [7] in 1903 gathered together six cases of progressive muscular atrophy of syphilitic origin, in two of which an autopsy was obtained. Subsequently with Lerouge [9] he considered the whole question

systematically in the light of seventy-five cases reported in the literature, and came to the conclusion that muscular atrophy of syphilitic origin was due to a diffuse vascular meningomyelitis. He included cases where signs were present of tabes dorsalis, of "general paralysis," or of lateral sclerosis, and explained the slightness of the meningeal changes found after death in such conditions by the gradual subsidence of the acute process. Nonne ([13], p. 418) takes much the same view and does not discuss the relation of these cases to "parasyphilis."

We pointed out [10] that cases of muscular atrophy of syphilitic origin could obviously be divided into two groups. Into the first group fell naturally those where clinical signs pointed to a widespread activity of the virus (cf. No. 36, p. 66), or where the Wassermann reaction and the signs of disease underwent a profound change for the better under treatment (cf. No. 146, p. 67). These belonged to the category fully described by Léri, and were instances of meningo-vascular syphilis. But we also showed that there was another group of syphilitic amyotrophies exactly analogous in their behaviour to tabes dorsalis, optic atrophy, or the so-called "parasyphilitic" lateral and combined scleroses. For not only do these patients show little improvement under anti-syphilitic treatment, but the Wassermann reaction remains materially unaltered in the cerebrospinal fluid.

Consider such an instance as the following:—

*A Case of Muscular Atrophy of Syphilitic Origin, associated with Abnormal Reaction of the Pupils. Positive Wassermann Reaction in the Cerebro-spinal Fluid.*

*Case* 198.—F. W., male, married, engineer's assistant: born 1868. In 1888, at the age of 20, this patient became infected with syphilis; he suffered from a chancre for which he was treated for a few weeks only. No manifestations of secondary syphilis followed and he remained in good health. He married in 1893 and three healthy children were born in 1894, 1897, and 1902, and are all alive: his wife has never miscarried.

In 1906, eighteen years after infection, he first complained of pain over the metacarpal of the right thumb and shortly after this the right index-finger dropped. Six months later he came under observation, and since this time has attended regularly at the London Hospital under the care of H. H. In 1908, he was an in-patient at the London Hospital and appeared to be a characteristic example of amyotrophic lateral sclerosis. He showed wasting of both upper extremities, most intense in the muscles of the hands and of the forearms, and greater on the right side than on the left; this wasting affected all the muscles of both upper extremities. Bilateral extensor plantar reflexes were obtained, but no ankle-clonus, and the knee-jerks were not increased. The pupils reacted to light and accommodation.

From 1908 until 1911, when he was admitted again to the London Hospital, the weakness and wasting of the upper extremities had progressed, the tongue became affected and the pupils no longer reacted to light. From 1911 until he received treatment with salvarsan, the condition progressed slowly; since then it has remained stationary.

In 1913 all the muscles of the neck, including the sternomastoids and the trapezii, were greatly wasted. The muscles around both shoulder-joints and the pectoralis major and minor, the serratus magnus and the latissimus dorsi were all intensely wasted. The affected muscles of the neck and shoulder regions showed fibrillary twitchings. Much wasting was present in both arms, more severe in the right than in the left. The muscles of the forearms were also gravely affected, but to a slightly less degree than the muscles of the upper arms. All the small muscles of the hands were atrophied and completely paralysed.

Movements of the right shoulder-joint were impossible; at the left shoulder-joint flexion and extension could be performed but not adduction and abduction. There was some movement at the right elbow and a little greater power at the left elbow. The patient could just flex the wrists on both sides and by means of the flexor sublimis and flexor profundus muscles could incompletely flex the fingers. When the fingers were extended he could just flex the distal phalanges by means of the lumbrical muscles. He could not bring his hands to his mouth unless he locked them together, placed his elbows against his trunk and jerked them up by means of movements of his back.

Except for the musculature of the neck and upper extremities, the other muscles supplied from the spinal cord were relatively well developed. There was no spasticity and no grave weakness of the legs.

The knee-jerks were normal and ankle-jerks were readily obtained. Both plantar reflexes gave an extensor response; on the right side the response was more readily elicited than on the left. The abdominal reflexes were unaffected.

Since 1907 he had suffered no pain, and no disturbance of sensibility could be discovered.

At no time had he experienced any difficulty in holding or passing water.

The movements of the lower portions of the spine were unaffected.

The pupils were unequal and excentric; the right was circular in outline and larger than the left, which was oval; they reacted extremely feebly to light, with a slow contraction, followed by an immediate dilatation, but both reacted well to accommodation.

The tongue showed severe, bilateral, almost symmetrical wasting, and fibrillary twitchings.

The movements of the eyes, jaws, face, palate, and larynx were unaffected.

Vision, hearing, smell, and taste were all normal, and the optic discs and fundi appeared healthy.

He was an extremely intelligent man, and showed no loss of memory, aptitude, or attention. He had never suffered from seizures or attacks of vomiting, and was not subject to headaches.

In January, 1913, the Wassermann reaction was found to be positive in the serum. In February, 1913, he was admitted as an in-patient at the National Hospital, Queen Square, where he was injected with two doses of 0·4 grm. of salvarsan.

On August 2, 1913, at the London Hospital, he was injected with 0·9 grm. of neosalvarsan.

On August 6, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.2.0.0.}{\text{cs.f. } 4.4.0.0.0.}$

He returned for further treatment in December, 1913, and was injected on December 3, on December 4, and again on December 8, with doses of 0·9 grm. of neosalvarsan.

On December 3, 1913, the Wassermann reaction was $\frac{\text{serum } 4.3.0.0.0.}{\text{cs.f. } 4.4.0.0.0.}$

On May 6, 1914, the Wassermann reaction was $\frac{\text{serum } 4.2.0.0.0.}{\text{cs.f. } 4.2.0.0.0.}$ and the cells numbered 3 per cubic millimetre.

Since the beginning of 1913 no new wasting and no fresh manifestations of any sort have developed.

This case corresponded in every detail with the usual description of amyotrophic lateral sclerosis, and yet the defective reaction of the pupils and the character of the Wassermann reaction in the cerebrospinal fluid shows that it belongs to the category of syphilis centralis. It is exactly analogous to a progressive case of tabes dorsalis or any other so-called "parasyphilitic" disease.

It is not difficult to differentiate such a case as this from those where the muscular atrophy is accompanied by other meningo-vascular lesions like No. 36 (p. 66). But we are still doubtful into which category No. 75 should be placed. This was a man, aged 36, who showed all the signs of a muscular atrophy of the upper extremities without any disturbance of sensation. The reflexes were unaffected, the pupils reacted extremely feebly to light, but there were no other abnormal signs pointing to lesions elsewhere in the nervous system. The Wassermann reaction on April 2, 1913, was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.0.0.}$ with 44 cells per cubic millimetre.

At first sight he is exactly analogous to No. 198, but after treatment with injections of neosalvarsan the atrophy ceased to progress and the strength of the positive reaction in the cerebrospinal fluid steadily diminished until on May 13, 1914, it was $\frac{\text{serum } 4.4.4.3.0.}{\text{cs.f. } 4.0.0.0.0.}$ and 3 cells per cubic millimetre.

*A Case of Muscular Atrophy of Syphilitic Origin associated with Abnormal Reaction of the Pupils. Positive Wassermann Reaction in the Cerebro-spinal Fluid.*

*Case* 75.—W. H., male, married, messenger; born 1877. He was in the Army in 1896, and again between 1900 and 1908; but although exposed to infection he can remember no venereal disease of any kind. In 1900, whilst in the Army, he had a bad throat lasting a few weeks only which was diagnosed as "diphtheria," but no other manifestations suggesting secondary syphilis.

In 1911 he began to lose power in the middle finger of his right hand. About three months later wasting started in the left arm, and within the space of a year had progressed to such an extent that he was unable to use either upper extremity.

On admission to the London Hospital on March 25, 1913, he was seen to be a well-developed man. All movements were impossible in the right upper extremity below the shoulder-joint and all the muscles, especially those of the hand, showed intense wasting. He could slightly flex the ring-finger of his left hand and evoke a feeble contraction of the flexors of the elbow, but otherwise all muscular power was lost. Movements at the right shoulder-joint were impossible; he could slightly contract the muscles of the left shoulder, but not with sufficient strength to produce any material change in the position of the limb. All the muscles of the neck were weaker than normal and somewhat wasted. There was no spasticity of the legs and the muscles of the trunk and lower extremities were normally developed.

The knee-jerks were brisk, the ankle-jerks were easily obtained, and both plantar reflexes gave a flexor response. The abdominal reflexes were normal. The wrist- and elbow-jerks could not be obtained.

He had suffered no pain, and no disturbance of sensibility could be discovered.

At no time had he experienced any difficulty in holding or passing his water.

Memory, attention and speech were unaffected and he did not suffer from headache, seizures, or attacks of vomiting.

Hearing, smell, taste and vision were normal, and the optic discs and fundi appeared healthy.

All ocular movements were natural. The pupils were unequal, the right larger than the left; both reacted extremely feebly to light with a slow, rhythmic response, but they reacted briskly to convergence and accommodation. The tongue showed no fibrillary tremor and the movements of the face, jaws, palate, and larynx were unaffected.

The blood pressure was 140 mm. of mercury and no abnormal signs were discovered in the heart, lungs, or abdomen. The urine contained neither albumen nor sugar.

On April 2, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{c.s.f.} \quad 4.4.4.0.0.}$ and the cells numbered 44 per cubic millimetre.

He was injected intravenously with doses of 0·9 grm. of neosalvarsan on April 5, April 12, and April 23, 1913.

He was readmitted for further observation on September 21, 1913, and although no material change had occurred in the manifestations of his nervous disease, his general condition had strikingly improved.

On September 24, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.3.}{\text{cs.f. } 4.3.0.0.0.}$

On September 24, 1913, he was again injected with 0·9 grm. of neosalvarsan and by May 13, 1914, the Wassermann reaction had become $\frac{\text{serum } 4.4.4.3.0.}{\text{cs.f. } 4.0.0.0.0.}$ and the cells now numbered only 3 per cubic millimetre.

Are we to look upon this patient as an example of syphilis centralis where the process is coming to a natural end, as may happen in tabes dorsalis, or is his muscular atrophy mainly the expression of meningo-vascular changes which have been influenced by treatment?

If both syphilis centralis and syphilis meningo-vascularis are manifestations of the same process in different anatomical structures, it is obvious that there can be no sharp line between them from the clinical aspect. Both can produce exactly the same clinical picture; it is only in those cases where additional signs point to accessory lesions, or where the Wassermann reaction in the cerebrospinal fluid becomes rapidly negative, that we can say with certainty whether or no the lesion is mainly meningo-vascular and can be influenced by drugs circulating in the blood-stream.

Thus, in conclusion, we believe that a form of amyotrophy exists which is exactly analogous to tabes dorsalis and primary optic atrophy; it may be associated with these conditions, or may occur alone. It is equally a manifestation of the activity of syphilis centralis, where the virus is acting on hypersensitized tissues, bathed in fluids which are only indirectly in connexion with the blood-stream.

### § 4.—*Optic Atrophy.*

Primary optic atrophy occurs so frequently as a complication of tabes dorsalis, that most observers have looked upon it as a manifestation of "parasyphilis." Thus Nonne ([13], p. 174) goes so far as to say that primary optic atrophy is always a sign that the case is one of tabes dorsalis, even if the knee-jerks are present, and he adds that it may exist alone for a long period before the appearance of any other signs. He gives a perfect instance of a woman, whom he had watched for eighteen years, with primary optic atrophy,

and no signs of tabes dorsalis or dementia paralytica had so far appeared.

To this we can add the following instance of a woman who began to lose her eyesight six years before admission to the Hospital. She was blind and showed all the signs of primary optic atrophy without any further evidence of disease of the nervous system.

*A Case of Primary Optic Atrophy where the Knee-jerks and Ankle-jerks were normal and there were no signs of Affection of the Posterior Columns of the Spinal Cord.*

*Case* 186.—J. A., female, widow; born 1853. In 1875, at the age of 22, she married her first husband, who died six years later from "asthma and bronchitis"; two out of three children, the issue of this marriage, were alive and well.

In 1892 she was married again to a husband who ultimately developed dementia paralytica and died insane in 1912. In this marriage she had two children, the first of whom, born in 1893, died of "wasting" at three months old, whilst the second, born two years later, was alive and healthy.

In 1905 she began to suffer from pains in the chest, but in view of the large gastric ulcer from which she ultimately died, these pains are of doubtful significance.

In 1907 she began to lose her eyesight. This loss of vision progressed slowly and culminated in 1910 in complete blindness.

When admitted in May, 1913, she was a sallow, anæmic woman, extremely intelligent, but totally blind. She suffered mainly from hæmatemesis and melæna which were due to a chronic ulcer of the stomach.

She showed no loss of memory or attention and had not suffered from any seizures or fits of any kind. Her speech was unaffected.

She was completely blind and the optic discs were in a condition of primary white atrophy. Hearing, smell and taste were unaffected.

The pupils were equal and reacted well to accommodation; they did not react to light in consequence of her blindness. All movements of the eyes, jaws, face, tongue, palate and larynx were performed normally. There was no tremor, no ataxia and she did not become unsteady when her eyes were closed.

No loss of sensation could be discovered to touch, pain or temperature, and she was able to appreciate perfectly the vibrations of a tuning-fork. Recognition of posture and passive movements was unaffected.

The knee-jerks and ankle-jerks were normal and both plantar reflexes gave a flexor response. The sphincters acted normally.

On May 5, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.3.0.0.}{\text{cs.f. } 4.4.3.0.0.}$ and the cells numbered 30 per cubic millimetre.

She died suddenly on May 30, 1913, of hæmatamesis and at the autopsy a large chronic ulcer of the stomach was found which had opened one of the coronal arteries.

The brain and spinal cord showed no signs of gummatous meningitis, but there was slight thickening of the leptomeninges; this was greatest in the neighbourhood of the optic tracts. Both optic nerves were atrophied but showed comparativly little infiltration. The cortex cerebri showed no abnormal changes. The posterior columns of the spinal cord were unaffected, except that, from the level of the 7th cervical segment upwards, a degeneration could be seen on both sides corresponding to a lesion of the 8th cervical nerve-roots. Sections of the 8th cervical spinal ganglion showed this root to be infiltrated. No changes were visible in the Weigert-Pal specimens pointing to tabes dorsalis and the other columns of the spinal cord appeared normal. There was no endarteritis or endophlebitis.

Thus it would seem that syphilis can produce degeneration of the optic nerve exactly analogous to the destruction of the posterior columns of the spinal cord in tabes dorsalis. Meningo-vascular syphilis may cause optic neuritis (No. 122, p. 16) and subsequent atrophy; but the changes dealt with in this section are manifestations of the activity of syphilis centralis, and they may occur apart from tabes dorsalis or any analogous condition.

### § 5.—*Gastric Crises.*

Uncontrollable attacks of vomiting bearing no relation to food are, like optic atrophy, so common a complication of tabes dorsalis that we are liable to forget that they are not an essential part of the disease. The gastric crises of tabes dorsalis probably arise in several different ways; but one form is obviously associated with irritation of the posterior nerve-roots in the thoracic region of the spinal cord. In these roots run the afferent fibres from the viscera, conducting their impulses to segmental centres in the spinal cord. Thus any inflammatory reaction of these posterior root-fibres in the thoracic region, whether inside or outside the spinal cord, will tend to set up reflex attacks of vomiting accompanied with violent root-pains around the trunk due to the coincident irritation of the somatic afferent fibres of the posterior roots.

In this section we are dealing with those gastric crises only which are accompanied by radicular pains and over-response to painful stimuli somewhere within the territory supplied by the sixth to the tenth thoracic roots. Some acute attacks of vomiting, occurring in tabes dorsalis, are not associated with these root-symptoms and, although they are true gastric crises of nervous origin, do not come within the group with which we are dealing.

Obviously any irritation of sufficient persistence and severity in

the lower thoracic region of the spinal cord will be liable to evoke paroxysmal attacks of reflex vomiting. We are so accustomed to associate these gastric crises with irritative destruction of the roots due to tabes dorsalis, that other possible causes for their appearance have been neglected. In Chapter III (p. 22) we have called attention to violent attacks of vomiting associated with irritation of the posterior roots by meningo-vascular syphilis; we gave an instance where the Wassermann reaction became negative within six months under the influence of injections of neosalvarsan.

When, however, the attacks are due to irritation of those same visceral afferent fibres by syphilis centralis, as for instance in cases of tabes dorsalis, the Wassermann reaction in the cerebrospinal fluid remains materially unaltered. The attacks are quite uninfluenced by the intravenous injections; in fact our experience has been that each injection is liable to be followed by a somewhat severe gastric crisis in patients with syphilis centralis.

Although these gastric crises are usually associated with some signs of affection of the posterior columns elsewhere than in the thoracic region, and the knee- and ankle-jerks are usually absent, this is not always the case. If no other signs are present the differential diagnosis is often very difficult apart from the behaviour of the cerebrospinal fluid. We have, therefore, chosen as our examples two cases where the deep reflexes were unaffected, and no other abnormal signs could be discovered except the defective reaction of the pupils.

The first example (No. 199) was a man aged 40 who, eleven years after infection, began to suffer from intense pain in the epigastric region associated with occasional attacks of vomiting. So severe was the pain that he was admitted under the surgeons as a case of duodenal ulcer. Sensibility to prick, and temperature was diminished over the area of the ninth and tenth thoracic roots on both sides accompanied by great over-reaction to any unpleasant stimulus; there was no demonstrable loss of sensation to cotton-wool. The left pupil did not react to light, but the deep reflexes were normal, and nothing pointed to any affection of the posterior columns of the spinal cord as far as the upper or lower extremities were concerned. The Wassermann reaction which was highly positive in the cerebrospinal fluid, remained entirely unaltered during the six months following treatment.

Our second case (No. 224) was almost identical in every way. The pupils reacted badly to light, but the deep reflexes were unaffected. Here, however, there was no diminution of sensibility, and all

tenderness and "hyperalgesia" disappeared between the attacks. In this patient also the highly positive Wassermann reaction in the cerebro-spinal fluid was unaffected by treatment.

*A Case of Gastric Crises with Defective Reaction of the Pupils and active Knee- and Ankle-jerks. Strongly Positive Wassermann Reaction in the Cerebro-spinal Fluid which was not affected by Treatment although the Number of Cells was greatly reduced.*

*Case* 199.—A. C., male, married, omnibus conductor; born 1874. This patient contracted syphilis in 1901 at the age of 27; he suffered from a chancre which healed without treatment and was not followed by any manifestations of secondary syphilis.

He married in 1897. His eldest child was born in 1899, the second, born in 1901, died three months later, the third was born in 1902, the fourth in 1903, the fifth in 1905, the sixth in 1906. He had been unhappy in marriage and he and his wife separated in 1908.

His health remained fair until 1908, when he attended at the Royal Ophthalmic Hospital, Moorfields, for some weeks complaining of "iritis." On November 1, 1912, whilst on the top of his 'bus, he was thrown against the side and hurt his left hand; the hand was bruised and did not seem to recover. Whilst still away from work, on December 15, 1912, he suffered from his first vomiting attack. The attack came on suddenly and seemed "like a bad attack of sea-sickness"; it was accompanied by intense pain in the abdomen and back and a "miserable feeling all over." The first attack lasted some twenty-four hours. Between December, 1912, and August, 1913, he suffered from six such attacks. They came on suddenly without warning, and, after lasting a variable period, usually a day and a half, ceased suddenly.

Each attack was more severe than its predecessor and was accompanied by much loss of weight. In December, 1912, he weighed 10 st. 6 lb. (66 kilos), in August, 1913, 8 st. 10 lb. (55 kilos).

He was admitted to the surgical side of the London Hospital on August 11, 1913, with the diagnosis that he was probably suffering from duodenal ulcer. On admission he was a spare man with thin limbs. He was miserable, inattentive and subject to attacks of weeping. His memory was fairly good and his speech unaffected. He slept badly. He had not suffered from headache or seizures. For the first six days after admission he vomited several times every day; these attacks of vomiting were only controlled by the free administration of morphia.

On admission he complained of shooting pains, tightness, and a miserable feeling of the lower abdomen and back, over an area corresponding to the distribution of the 9th and 10th thoracic roots on both sides. This area was tender to pressure and responded excessively to the dragged point of a pin. He said that the point here seemed "dull" and "different" although it "hurt more," and that the hot and cold tubes were "altered" and "not so hot,"

"not so cold"; and yet the sensation evoked by cotton-wool was "the same" over this area as elsewhere over the body. On the extremities there was no sensory loss and the vibrations of a tuning-fork were well appreciated everywhere.

His muscular power was poor, but his gait was unaffected and Romberg's sign was not obtained. There was no ataxia of the hands, no local paresis or atrophy of any group of muscles, and no hypotonia.

The knee-jerks and ankle-jerks were readily elicited and both plantar reflexes gave a flexor response. The abdominal reflexes were unaffected.

He had experienced some difficulty in passing his water and often had to wait for ten or more minutes before the stream would come.

The ocular movements were unimpaired. The pupils were of pin-point size, regular in outline and well centred; the left did not react to even the brightest lights, the right reacted sluggishly; in bright light neither pupil reacted to accommodation, but if he was kept in the dark a slight reaction was obtained. The movements of the face, jaws, palate, larynx and tongue were unaffected. The functions of the special senses were unimpaired and the optic discs and fundi appeared natural.

On August 20, 1913, the Wassermann reaction was $\frac{\text{serum}\ 4.4.4.4.0.}{\text{c.s.f.}\ 4.4.4.4.0.}$ and the cells numbered 40 per cubic millimetre.

On August 15, on August 20, and again on August 24, he was given intravenous injections of 0·9 grm. of neosalvarsan.

After treatment the vomiting ceased, the patient's mental condition brightened, the sensory over-reaction became less and its limits more difficult to define; the patient declared that he felt "better than he had felt for months."

He returned for further treatment and investigation in February, 1914. At this time he was more contented and less worried. He said that since his discharge he had found great difficulty in avoiding alcohol and in keeping "straight." Since his discharge he had suffered from attacks of vomiting lasting about a day, coming on at intervals of about a week or a fortnight and leaving his abdomen sore. His physical state was little altered except that the upper abdominal muscles now appeared wasted and bulged when he lifted his head from the bed, and the plantar responses were no longer definitely flexor.

On February 19, 1914, the Wassermann reaction was $\frac{\text{serum}\ 4.4.4.4.0.}{\text{c.s.f.}\ 4.4.4.4.0.}$ but the cells numbered 4 per cubic millimetre only.

*A Case of Gastric Crisis with Argyll-Robertson Pupils and active Knee- and Ankle-jerks. Strongly Positive Wassermann Reaction in the Cerebro-spinal Fluid which was not affected by Treatment.*

*Case* 224.—P. H., male, married, mercantile marine service; born 1883. In the summer of 1911, he began to suffer from apparently causeless attacks of vomiting, unaccompanied by abdominal pain. For the first two months the

attacks came on once or twice a week and lasted two or three days. They started and ended suddenly. Towards the end of the year 1911 the attacks became less frequent: in August, 1912, however, they again became more numerous and of longer duration. For a week or more he would vomit after every meal; this was followed by a period of normal health, succeeded in turn by another attack. At this time the vomiting was effortless and was not preceded by nausea or retching. It was not accompanied by flatulence, pyrosis or indigestion and he was not constipated between the attacks.

On August 28, 1913, a violent attack started which lasted continuously for a fortnight; in this attack for the first time pain became a noteworthy feature: the abdomen in the region of the epigastrium became sore and every few minutes a pain shot from this portion of the abdomen round the trunk into the back. This made him extremely miserable and depressed. During the attack he lost flesh and his weight fell from 11 st. 9 lb. in 1911 to 9 st. 7 lb. in September, 1913, a loss of 30 lb. (or 13½ kilos).

He denied all venereal infection, but admitted exposure as a young man. Whilst abroad in 1900 he suffered from "yellow fever" and also from "cholera." He married in 1909, and in 1911 a child was born which is healthy.

On September 13, 1913, he was admitted to the London Hospital for operation under the care of Mr. James Sherren, complaining of attacks of vomiting and an irritable feeling in the upper part of the abdomen and back; he said he felt worried and was mentally very depressed.

No abnormal physical signs were discovered in the abdomen, heart, arteries or lungs. A test breakfast of toast and tea showed the presence of 0·08 per cent. free hydrochloric acid and a total acidity of 42. Radiological examination of the stomach showed that it was not dilated and emptied itself rapidly.

When transferred to the medical side he was loquacious, introspective and inattentive. His memory was somewhat defective, but he gave his history clearly. He said that he forgot little details of his work, and that his "memory was not what it was." His speech was unaffected and headache was not a noticeable feature. After admission he vomited many times; the attacks of vomiting were sudden and bore no relation to food, but were accompanied by much abdominal pain with superficial and deep tenderness of the upper abdomen on both sides. He vomited many times each day for eight consecutive days. He had suffered from no other form of paroxysmal attacks or from epileptiform seizures.

The pupils were unequal, the right much wider than the left: the left just flickered on stimulation with intense lights, whilst the right showed no reaction, but both reacted well to accommodation. No other abnormal signs were discovered in the territory of the cranial nerves.

Taste, smell, hearing and vision were unaffected, and the fundi showed no abnormal appearances.

Motion was completely unaffected and no disturbance of sensibility was present except during the attacks and for three days afterwards. Posture and

passive movement and the vibrations of the tuning-fork were well recognized on both legs. During the attacks of vomiting the areas of skin corresponding to the peripheral distribution of the sixth, seventh, eighth, and ninth thoracic nerve-roots on both sides became tender and over-reacted to pinching and the dragged point of a pin, but over these areas no sensory loss of any kind could be discovered.

The knee-jerks and ankle-jerks were readily obtained and the plantar reflexes on both sides gave a flexor response. The abdominal reflexes and the wrist- and elbow-jerks were normal.

He suffered from no trouble in holding or passing his urine or motions.

The urine contained a trace of albumen and a small quantity of pus, but the quantity secreted and the specific gravity were normal.

The Wassermann reaction on September 19, 1913, was $\frac{\text{serum}\ 4.4.4.4.4.}{\text{cs. f.}\ 4.4.4.0.0.}$

He was injected on September 24, October 1, and October 13, 1913, with doses of 0·9 grm. of neosalvarsan. After each injection he suffered from a violent gastric crisis, lasting about forty-eight hours, with slight pyrexia to 100° F. (38·3° C.). The quantity of urine excreted fell from 42 oz. to 22 oz. on an average. As soon as the vomiting ceased he rapidly regained the weight which he had lost during the attack.

He was readmitted for investigation on April 17, 1914. The signs of disease were unchanged and, although the attacks were as numerous and severe as before, his general condition between them had improved greatly.

On April 23, 1914, the Wassermann reaction was $\frac{\text{serum}\ 4.4.4.4.3.}{\text{cs.f.}\ 4.4.4.1.0.}$ and the cells numbered 13 per cubic millimetre.

He was treated with 0·9 grm. of neosalvarsan on April 21, 1914. After this injection a violent "gastric crisis" set in and lasted until May 1. On April 23 he vomited three times, on the 24th six times, on the 25th six times, on the 26th twice, on the 27th six times, on the 29th four times, on the 30th once, and on May 1 once. The whole abdomen between the peripheral distribution of the 6th thoracic and the 1st lumbar nerve-roots on both sides was tender and reacted excessively to the dragged point of a pin; this area of tenderness gradually disappeared and by May 1 had almost entirely gone. During the attack he took hardly any food, he wasted rapidly and cried out for morphia. Whenever he came round from the effect of the drug, he was extremely miserable and immediately complained of a feeling of sickness, retched and vomited. The attack ended suddenly and left him extremely weak.

By May 6, he felt well again and was injected with 0·9 grm. of neosalvarsan. On this day and again on May 9 he received a similar dose; neither injection was followed by any ill-effect.

### § 6.—*Epileptic Manifestations.*

Fournier ([4] p. 238) called attention to a form of epilepsy liable to appear many years after syphilitic infection, which was entirely refractory to anti-syphilitic treatment. This he believed to be a

manifestation of "parasyphilis." Nonne ([13] p. 284) entirely agrees with this description and accepts "parasyphilitic" epilepsy as a condition comparable to tabes dorsalis and dementia paralytica. He carefully differentiates it, on the one hand from cerebral syphilis, and on the other from the seizures which may herald the early stages of dementia paralytica.

But all authorities agree that "gummatosis" affecting the cerebral cortex may produce a condition which cannot be materially improved by anti-syphilitic remedies; clinically it cannot be differentiated from this "parasyphilitic" epilepsy, except by the behaviour of the Wassermann reaction in the cerebrospinal fluid. For, as a rule, the cerebrospinal fluid in cases of chronic meningo-vascular syphilis of the cortex yields a negative reaction, if there are no spinal or bulbar complications; but any case diagnosed as "parasyphilitic" epilepsy must follow the rules we have laid down and give a positive reaction in the cerebrospinal fluid, which is not materially affected by anti-syphilitic treatment.

We have seen one case only (No. 66) which fulfilled these conditions. The disease arose on a basis of a juvenile infection and is interesting from the presence of Argyll-Robertson pupils. It illustrates the long duration of the disease and the persistence of the positive Wassermann reaction in the cerebrospinal fluid in spite of treatment. At the end of over two years the strength of the reaction was almost the same as on the first observation.

*A Case of Epilepsy in a Patient with Juvenile Syphilis. The Wassermann Reaction was Positive in the Cerebrospinal Fluid and the Cells were in excess. Treatment improved her General Condition, but did not stop the Fits or materially change the Strength of the Wassermann Reaction.*

*Case* 66.—F. G., female, single; born 1889. This patient has been under the care of H. H. since 1904 suffering from epileptiform attacks. In 1900, at the age of 11, she developed fits, which have continued ever since in spite of treatment. The attacks come on without warning, she passes water, falls, and has not infrequently hurt herself. Throughout she is completely unconscious, and she sleeps after the attack. Usually two or more fits occur in rapid succession.

There is no family history of epilepsy. Her mother married in 1878. Of this marriage there have been (i) a child born in 1879, who died at the age of 14 months of "consumption of the bowels"; (ii) a child born in 1881, who died aged 12 months of "scarlatina"; (iii) a healthy female, born in 1885, now married, with a healthy child, born in 1911; (iv) a healthy male, born May, 1887; (v) the patient, born April, 1889; (vi) a male born in 1891, living and healthy; (vii) a child who died at the age of 12 months of "summer diarrhœa"; and (viii) a child who survived and is healthy, born in 1895.

The patient was a full-time, healthy child, born with a breech presentation after a difficult labour.

In 1890, at the age of 18 months, she developed a syphilitic rash and was treated for eight months with mercury by the mouth. Under this treatment she developed into a "fine healthy child."

Before the onset of the nervous manifestations, her only illness was an attack of measles in 1897.

In 1897, at the age of 10, she reached Standard iv; then she began to "go wrong." She became restless, irritable, and clumsy in action and subsequently began to suffer from epileptiform attacks.

In 1903 she attended the ophthalmic department of the London Hospital under the care of Mr. Roxburgh for interstitial keratitis, and was transferred by him to the care of Dr. Head.

She is short and broad, 4 ft. 10 in. (146 cm.) in height with a narrow forehead and pegged teeth. Scars are visible at the angles of the mouth and she has the characteristic appearances of a case of juvenile syphilis.

Her attention and memory are poor, but she shows no gross signs of dementia. Her speech is unaffected, and excepting after an attack, she is not liable to headaches or vomiting.

She is somewhat deaf. The corneæ show faint nebulæ, but the fundi appear natural.

The pupils are usually equal and of fair size, but they do not react to light: they react well to accommodation. The face is expressionless and the tongue on protrusion comes out straight and is held steadily.

The knee-jerks and other reflexes including the plantars are normal, except after a series of convulsions.

Motion, sensation and the action of the sphincters are entirely unaffected.

In September, 1911, with "heart antigen" the Wassermann reaction was $\frac{\text{serum}\ \ 0.0.0.0.0.}{\text{cs.f.}\ \ \ 4.2.1.0.0.}$[1] and the cells were in excess. At this time she was thought to be a case of juvenile dementia paralytica and was not injected with salvarsan.

On June 4, 1913, the Wassermann reaction was $\frac{\text{serum}\ \ 4.4.2.0.0.}{\text{cs.f.}\ \ \ 4.4.4.4.0.}$ and the cells numbered 40 per cubic millimetre.

On June 6, 1913, she was given 0·9 grm. of neosalvarsan intravenously, and similar doses were administered on the 13th and 18th of that month.

After the injections her general condition improved and for the first time she began to menstruate regularly. The treatment, however, had no effect on the nature or the frequency of the attacks.

On December 4, 1913, the Wassermann reaction was $\frac{\text{serum}\ \ 4.4.1.0.0.}{\text{cs.f.}\ \ \ 4.4.0.0.0.}$ and the cells numbered 1 per cubic millimetre.

[1] This is the only occasion in this paper when we have quoted a Wassermann reaction obtained with this antigen. In all other instances, including the other estimations in this patient, the technique was that laid down by Fildes and McIntosh [3].

TABLE F.—TO SHOW THE ABSENCE OF CHANGE IN THE WASSERMANN REACTION AFTER TREATMENT IN CASES OF SYPHILIS CENTRALIS.

| No. of case | Before treatment | After treatment | Intervening period | Treatment |
|---|---|---|---|---|
| **DEMENTIA PARALYTICA.** | | | | |
| 20 (Autopsy) .. | 4.4.4.3.1.<br>4.4.4.4.1. | 4.4.4.3.2.<br>4.4.4.2.0. | 45 weeks | 3 doses of 0·9 grm. of neosalvarsan |
| 32 (p. 92) .. | 4.4.4.2.1.<br>4.4.4.3.2. | 4.4.4.4.0.<br>4.4.4.2.0. | 63 ,, | 2 doses of 0·6 grm. of salvarsan |
| 90 (Autopsy) .. | 4.4.4.4.2.<br>4.4.4.4.0. | 4.4.4.4.4.<br>4.4.3.0.0. | 23 ,, | 3 doses of 0·9 grm. of neosalvarsan |
| 200 (p. 95) .. | 4.4.4.4.3.<br>4.4.4.4.4. | 4.4.4.4.4.<br>4.4.4.4.4. | 55 ,, | 4 doses of 0·9 grm., 1 of 0·2 grm. and 3 of 0·3 grm. of neosalvarsan and 4 intrathecal injections of 10 c.c. of "salvarsanized serum" |
| 230 (Autopsy) .. | 4.4.4.4.4.<br>4.4.4.4.4. | 4.4.4.4.4.<br>4.4.4.4.4. | 15 ,, | 3 doses of 0·9 grm. of neosalvarsan |
| **JUVENILE DEMENTIA PARALYTICA.** | | | | |
| 197 .. .. | 4.4.4.4.4.<br>4.4.4.2.0. | 4.4.4.4.0.<br>4.4.4.4.0. | 40 weeks | 4 doses of 0·6 grm. of neosalvarsan |
| **TABES DORSALIS.** | | | | |
| 37 (p. 107) .. | 4.4.2.0.0.<br>4.4.3.1.0. | 4.4.4.2.0.<br>4.4.2.0.0. | 47 weeks | 3 doses of 0·9 grm. of neosalvarsan |
| 142 .. .. | 4.4.4.0.0.<br>4.4.4.0.0. | 4.4.4.4.2.<br>4.4.1.0.0. | 77 ,, | 2 doses of 0·9 grm. of neosalvarsan |
| 150 .. .. | 4.4.4.4.2.<br>4.4.3.0.0. | 4.4.4.4.4.<br>4.4.1.0.0. | 47 ,, | 3 doses of 0·9 grm. of neosalvarsan |
| **MUSCULAR ATROPHY.** | | | | |
| 198 (p. 110) .. | 4.4.2.0.0.<br>4.4.0.0.0. | 4.2.0.0.0.<br>4.2.0.0.0. | 41 weeks | 2 doses of 0·4 grm. of salvarsan and 4 doses of 0·9 grm. of neosalvarsan |
| 75 (p. 113) .. | 4.4.4.4.4.<br>4.4.4.0.0. | 4.4.4.3.0.<br>4.0.0.0.0. | 58 ,, | 4 doses of 0·9 grm. of neosalvarsan |
| **GASTRIC CRISES.** | | | | |
| 199 (p. 118) .. | 4.4.4.4.0.<br>4.4.4.4.0. | 4.4.4.4.0.<br>4.4.4.4.0. | 29 weeks | 3 doses of 0·9 grm. of neosalvarsan |
| 224 (p. 119) .. | 4.4.4.4.4.<br>4.4.4.0.0. | 4.4.4.4.3.<br>4.4.4.1.0. | 31 .. | 3 doses of 0·9 grm. of neosalvarsan |
| **"PARASYPHILITIC" EPILEPSY.** | | | | |
| 66 (p. 123) .. | 4.4.2.0.0.<br>4.4.4.4.0. | 4.4.1.0.0.<br>4.4.0.0.0. | 26 weeks | 3 doses of 0·9 grm. of neosalvarsan |

## [B] The Effect of Treatment on the Wassermann Reaction in Syphilis Centralis.

It is universally recognized that syphilis centralis, in its acute forms, tends to produce a strongly positive reaction in the cerebrospinal fluid, and throughout the previous half of this chapter we have given many instances in support of this belief.

This positive reaction is not materially affected by doses of neo-salvarsan sufficient, in cases of meningo-vascular syphilis (Chapter IV, p. 84), to be capable of converting a positive into a negative reaction in the cerebrospinal fluid within a few months.

We have gathered together fourteen cases of the various forms assumed by syphilis centralis, to form Table F, and it will be evident how little change occurs after treatment. In a few cases, such as those of tabes dorsalis and muscular atrophy, the positive reaction in the cerebrospinal fluid is occasionally slightly less strong in the later examination; but there is nothing to show that this was the direct and immediate result of the treatment. We have put together, on Table G, four cases of tabes dorsalis where no anti-syphilitic treatment of any kind was given; of these two showed the same slight diminution in the strength of the positive Wassermann reaction in the cerebrospinal fluid.

Table G.—Tabes Dorsalis.

| No. of case | First observation | Subsequent observation | Intervening period | Treatment |
|---|---|---|---|---|
| 30 .. .. | 4.1.0.0.0.<br>4.4.4.4.0. | 4.0.0.0.0.<br>4.4.4.0.0. | 79 weeks | None. |
| 58 .. .. | 4.3.1.0.0.<br>4.4.4.0.0. | 4.4.4.1.0.<br>4.4.4.2.0. | 106 ,, | ,, |
| 70 .. .. | 4.4.4.2.0.<br>4.3.0.0.0. | 4.4.4.4.4<br>4.4.0.0.0. | 81 ,, | ,, |
| 131 .. .. | 4.3.2.1.0.<br>4.4.4.3.1. | 4.4.4.4.4.<br>4.4.0.0.0. | 114 ,, | ,, |

We believe that syphilis centralis is the reaction of the hypersensitized neuroglia and essential tissues of the nervous system to the activity of the syphilitic virus. In many cases this tissue reaction tends to come to an end with time (p. 102), and provided the patient is not killed by the severity of the active disease, he may settle down into a case of chronic degeneration of certain parts of the nervous

system. His signs and symptoms are due to the after-effects of the tissue reaction and not to any active process. The Wassermann reaction in the cerebrospinal fluid also tends slowly to become negative and we therefore look upon the slight diminution in strength of the positive reaction in some of the cases on Tables F and G as further evidence of this tendency for the active process to die out in the tissues of the central nervous system.

## Chapter VI.—Mixed Forms.

We have put forward the view that there is no essential difference pathologically between the nature of meningo-vascular and central syphilis; both are due to the action of the virus on tissues already rendered hypersensitive to a varying degree. The only difference lies in the site of the lesion, and consequently in the character of the tissues attacked. Moreover, the meninges and vessels are exposed to the action of drugs in the circulatory system, whilst the essential elements of the brain and spinal cord are only indirectly affected by the contents of the blood-stream.

If these views are correct, it is obvious that cases must exist where the foci of spirochætosis affect the meninges, the vessels and the essential structures of the nervous system at the same time. Such cases would show features reminiscent of the behaviour on the one hand of syphilis meningo-vascularis, on the other of syphilis centralis. These we speak of as "mixed forms."

Thus, for instance, No. 159, when he first came under our care, showed signs pointing to basal meningitis and disease of the cerebral vessels; for, in addition to his mental instability, a well-marked nystagmus was present, and the right half of the palate was paretic. But, although these signs disappeared under treatment, the positive Wassermann reaction in the cerebrospinal fluid remained uninfluenced, and his general condition steadily deteriorated. It is interesting to notice in this case that the symptoms of disease of the central nervous system came on within three years of infection.

The second case (No. 280) was thought to be one of dementia paralytica, in spite of the short period that had elapsed since infection. Speech was affected, face, tongue, and hands were tremulous, and the patient had suffered from several seizures. He had been treated with mercury and with intravenous injections of salvarsan before he came under our care in August, 1912; but his Wassermann reaction was completely positive in the cerebrospinal fluid.

He improved greatly under treatment, and is now able to take part in the ordinary occupations of daily life. His memory is good, and he can even solve complicated problems in calculation. But his speech is still affected, and a good deal of tremor remains in the face and tongue. At the same time the Wassermann reaction in the cerebrospinal fluid is still almost completely positive, and shows no material change in spite of energetic anti-syphilitic treatment.

In No. 125 our third instance of these mixed forms, the obvious root affections, accompanied at one time by herpes zoster, pointed to active disease of the meninges. On the other hand, the absent knee-jerks, ataxy, and other signs of profound affection of the posterior columns pointed to central disease. The patient improved greatly under treatment, and at first the highly positive Wassermann reaction in the cerebrospinal fluid yielded somewhat to treatment. But at the end of over twelve months he still gave a strongly positive reaction in the cerebrospinal fluid: the root-symptoms and weakness in the legs had disappeared, but he now exhibited all the signs of tabes dorsalis. Here, then, was an instance where one aspect of the disease showed great improvement, but the signs of deeper affection of the nervous system remained unaltered.

*A Case of Syphilis of the Central Nervous System appearing Three Years after Infection. A Strongly Positive Wassermann Reaction and Great Pleocytosis in the Cerebrospinal Fluid which were not influenced by Treatment.*

*Case* 159.—W. G. T., male, single, surveyor: born 1878. In 1908, at the age of 30, this patient contracted a "running"; at first this was thought to be a simple gonorrhœa, but a few months later he suffered from a series of bad throats and was then treated regularly for eighteen months with mercurial pills.

From 1908 until the spring of 1911 his health was fairly good. Then his memory began to fail and he found that he was no longer able to do his work up to his old standard and that he was easily worried with the details of business. In January, 1912, insomnia became troublesome and he suffered from a "continual muzziness in the head," "a sort of headache at the back of the eyes with a buzzing noise and discomfort in the ears." He became more worried, more emotional and began to lose flesh. In June, 1912, he went to camp with the Territorials: on his return he had a "complete nervous breakdown" with depression accompanied by neurasthenic symptoms. He became unable to think consecutively and felt unequal to any but routine work. During the next six months he remained in much the same condition; the only new symptom which developed during this time was some difficulty in starting micturition.

He first came under our observation on January 18, 1913. On admission

memory, especially technical memory, was defective; he was depressed and introspective. His attention was good and his speech unaffected. He complained of noises in the head and of a feeling of fulness which was not accompanied by any pressure-tenderness of the scalp. He had suffered from no seizures and from no attacks of vomiting.

Hearing, smell, taste, and vision were unaffected and the optic discs and fundi appeared healthy.

A well-marked nystagmus was present; this was best observed when the patient looked to the extreme left and was more noticeable in the left eye than in the right. The pupils were equal and well centred; both reacted to light and accommodation; on the right side, however, the reaction was badly sustained. There was no diplopia or ptosis and the facial movements were natural. On phonation the uvula was drawn up to the left, but the movements of the tongue and larynx were unaffected and there was no wasting of the trapezius and sternomastoid muscles.

The gait and movements of the hands were unaffected. There was no alteration in the muscular tone of the extremities and no local muscular wasting was present.

The patient complained of no spontaneous pains in the trunk and no interference with sensation was discovered.

The knee-jerks and ankle-jerks were readily obtained, but on the right side the plantar reflex gave an extensor, on the left a flexor response. The abdominal reflexes and the wrist- and elbow-jerks were natural.

Whilst under observation he experienced no difficulty in holding or passing water; but before his admission he had had difficulty in starting the act of micturition and occasionally he had wetted himself.

On January 22, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.3.0.}{\text{cs.f. } 4.4.4.4.1.}$ and the cells numbered 50 per cubic millimetre.

He was injected on January 25, January 31, and February 5, 1913, with doses of 0·9 grm. of neosalvarsan.

After this treatment he improved considerably, regained confidence and went back to his old employment. He returned for further investigation in October, 1913. At this time his physical state was closely similar to that shown in the previous January, except that the nystagmus had disappeared and his palate moved normally. On October 14, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.0.}{\text{cs.f. } 4.4.4.4.4.}$ and the cells numbered 40 per cubic millimetre.

He was injected with 0·9 grm. of neosalvarsan on October 24, and again on November 14 and November 18, 1913.

On June 8, 1914, he stated that he was more easily tired. He had lost his employment, but had just returned from training in camp. There he acted as sergeant and led his battery, but was obliged to go into hospital, at least on one occasion, "because he felt queer." His speech was now affected and there was much tremor of the face and lips. His handwriting was only slightly

affected. All his reflexes, superficial and deep, were now normal. His pupils reacted sluggishly to light, the right better than the left. The palate moved normally. He had no difficulty with micturition.

The Wassermann reaction on June 10, 1914, was $\frac{\text{serum } 4.4.4.4.2.}{\text{cs.f. } 4.4.4.4.4.}$ and the cells were 38 per cubic millimetre.

On June 9, 1914, he was given 0·9 grm. of neosalvarsan without subsequent rise of temperature or any immediate ill results. On June 11, he was given a similar dose. Eight hours later, without rise of temperature or other signs of reaction, he became muddled, looked wildly around the ward, lost his power of counting money and ordered the patients about in a lordly manner. This change lasted until June 14, when it passed away, leaving him in the condition in which he was admitted.

*A Case where Signs and Symptoms resembling those of Dementia Paralytica came on within four and a half years of Infection in a man aged 28. The Condition of the Patient improved greatly under Treatment, although the Wassermann Reaction in the Cerebrospinal Fluid remained almost Completely Positive.*

*Case* 280.—V. W., single; born 1884. In March, 1906, he was infected with syphilis and suffered from a chancre, followed by sore throats, but from no other symptoms. He took mercury by the mouth for two and a half years.

In June, 1910, he suddenly fell unconscious in the street, and was convulsed. After this he received a series of injections of mercury cream into the buttock.

On September 14, 1910, he consulted an ophthalmic surgeon, who found his left pupil inactive to light, whilst the right reacted well. This remained constant for many months and as the Wassermann reaction in his serum was positive he was injected with 0·3 grm. of salvarsan on April 13, 1911, 0·4 grm. on April 18, and 0·6 grm. on May 19.

He was operated on for piles on August 15, 1911, so clumsily that a stricture of the rectum was produced, associated with inability to hold his motions from damage to the sphincter ani.

On December 29, 1911, he was again injected with 0·6 grm. of salvarsan.

He was admitted to the Naval Hospital, in January, 1912, because of the trouble with his rectum consequent on the operation. Whilst there he suffered from transitory loss of speech, and on several occasions his arms and legs became "numb and useless."

During June, 1912, he had a second attack in which he fell and became unconscious.

When he first came under our care in August, 1912, his memory was extremely defective, and he was confused; he could not remember dates, muddled the years, and had forgotten the ships in which he had served. Although very highly educated he could not multiply, and found great difficulty with figures. His writing was tremulous, syllables were omitted

and words misspelt, when he wrote to dictation. Speech was thick, slurred and tremulous.

He walked slowly, but there was no ataxy of upper or lower extremities. His hands were tremulous.

The right pupil reacted sluggishly, if at all, to light, and tended slowly to contract and dilate independently of stimulation. It was smaller than the left pupil, which now reacted normally. There was no ocular paralysis, diplopia or nystagmus. The face was flattened; lips and tongue were tremulous.

The knee-, ankle-, and wrist-jerks were exaggerated: no ankle-clonus could be obtained and both plantar reflexes gave a flexor response.

Sensation was not disturbed, vision, hearing and smell were unaffected and both optic discs were normal.

The sphincters now reacted normally, but he was extremely careless about cleansing himself after passing a motion.

His Wassermann reaction on August 8, 1912, was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.4.4.}$

On November 26, 1913, he was admitted to the London Hospital, in much the same condition except that both pupils now reacted to light, and the tremor of the face and tongue was less evident. His mental state had considerably improved. The Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.4.4.}$ and 14 cells per cubic millimetre.

He was injected on November 26, 1913, with 0·9 grm. of neosalvarsan. On February 24 and 26, 1914, he received two doses of 0·9 grm. of neosalvarsan.

Since November, 1913, his symptoms have steadily improved. He now (June, 1914) spends most of his time yachting and his golf handicap is down to 12. Memory has greatly improved, and he is no longer irritable or emotional. Coarse tremor of the lips and tongue is still present but his speech has considerably improved. Both pupils react sluggishly to light: the right is now larger than the left. No other abnormal signs can be discovered. But in spite of this improvement in symptoms, the Wassermann reaction is $\frac{\text{serum } 4.4.4.4.1.}{\text{cs.f. } 4.4.4.4.3.}$ and 9 cells per cubic millimetre.

*A Case of Ataxy with much loss of Sensation in both Lower Extremities and Argyll-Robertson Pupils. Loss of all Reflexes superficial and deep below the Groins. Herpes Zoster. Strongly Positive Wassermann Reaction in the Cerebrospinal Fluid which became slowly reduced after Intensive Treatment.*

*Case* 125.—F. P., male, married, coachman; born 1881. In 1902, this patient contracted a "running" for which he received no treatment. At no time had he suffered from any sore or rash, but some time later he began to complain of bad throats which lasted "a few months."

He married in 1906 and his wife has had two children, born in 1907 and 1910, and no miscarriages.

In September, 1912, he developed an "influenza," in which he suffered from running from the nose and eyes, pains all over and low spirits. After this attack he never "seemed himself." About the middle of October, 1912, he first experienced difficulty in starting the act of micturition, which ended in incontinence of urine from overflow. Towards the end of October he began to complain of intense, dull, heavy pains in the legs and calves. The pains were worse in the left leg than in the right, and were always worse at night than by day. Then his arms became affected with a sort of "cramp" which kept him from using his hands. On November 16, 1912, he took to his bed. On November 20, on attempting to get out of bed he found that he was totally unable to stand. After this date he completely lost sensation in both lower extremities and control over his sphincters.

On December 8, 1912, when admitted to the London Hospital, the patient was a pale, thinly covered man. On the front of the shins were thin tissue-paper scars. The right pillar of the fauces was adherent to the back of the pharynx and both pillars were much scarred. No scar could be found on the penis.

Memory, attention and speech were little affected. He complained of no headache. He had suffered from no seizures or attacks of vomiting.

The movements of the eyes were normal. The pupils were of pin-point size, equal and well centred; neither reacted to the most intense light, but both reacted slightly to accommodation and convergence. In the territory of the cranial nerves no other abnormal signs were present.

The alignment of his fingers and hands was good. He could not stand, but could just move his legs. All the muscles of the lower extremities were flaccid and the calves were wasted, although the thighs were fairly developed.

He complained of spontaneous shooting pains in the legs, and of a tight girdle sensation just below the level of the umbilicus. Over the areas of skin supplied by the eleventh and twelfth thoracic nerve-roots the patient was tender and reacted excessively to the dragged point of a pin. There was much loss to all sensory tests below the level of the groins. The loss to pain, to heat and to cold was greater on the right leg than on the left. Ice and water at 50° C. could be distinguished on both legs, but he was uncertain in his answers to the intermediate degrees of temperature, more especially to those between 20° C. and 40° C. The impairment to painful stimuli affected both pressure-pain and the painful aspect of the prick of a pin. His answers to examination with the tuning-fork and to the tests for posture and passive movement were extremely bad; they were worse on the left leg than on the right, yet whenever any answer was obtained it was correct. The contact of cotton-wool was appreciated on both legs, but there was more uncertainty on the right than on the left.

The knee-jerks and ankle-jerks were completely abolished, and no plantar responses could be obtained to stimulation of the soles of the feet or the front of the ankles and shins. The upper and lower abdominal reflexes were obtained, but the cremasteric reflexes were abolished. The wrist- and elbow-jerks were readily elicited.

On admission, retention of urine necessitated the use of a catheter; on the sixth day after admission he began to pass urine naturally.

No abnormal physical signs were discovered in the heart, lungs, abdomen or urine.

On December 11, 1912, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.4.3.}$ and the cells numbered 5 per cubic millimetre. He was injected with doses of 0·9 grm. of neosalvarsan on January 4, January 14, and again on January 22, 1913.

On February 7, 1913, he was discharged from Hospital. At this time he had little or no knowledge of where his legs were, he could not walk and could only stand with difficulty.

He was readmitted for further treatment on April 21, 1913. At this time he was able to walk. He was extremely ataxic, more especially with the left leg and Romberg's sign was present. The knee-jerks, ankle-jerks and the plantar reflexes could not be obtained. He complained of precipitancy in micturition and of shooting pains in the old tender area (eleventh and twelfth thoracic nerve-roots) and also in the arms and axillæ. Hyperalgesia was present over the distribution of the third, tenth, and eleventh thoracic roots on both sides. There was still much sensory loss on both lower extremities to all tests except cotton-wool.

On April 23, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.4.}{\text{cs.f. } 4.4.4.0.0.}$ and the cells numbered 3 per cubic millimetre. He was

injected on April 25, 1913, with 0·12 grm. of neosalvarsan.
" " " 29, " " 0·15 " " "
" " May 2, " " 0·15 " " "
" " " 5, " " 0·3 " " "
" " " 9, " " 0·3 " " "
" " " 13, " " 0·3 " " "
" " " 16, " " 0·3 " " "
" " " 19, " " 0·3 " " "
" " " 23, " " 0·3 " " "
" " " 27, " " 0·3 " " "

making in all 2·52 grm.

On September 1, 1913, he developed herpes zoster of the 9th thoracic root on the left side (*vide* fig. 2, p. 24).

On September 7, 1913, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.0.}{\text{cs.f. } 4.4.2.0.0}$

He was injected with 0·9 grm. of neosalvarsan on September 8, 1913.

After this treatment the improvement in function continued, but the Argyll-Robertson pupils, the absence of the knee-jerks, ankle-jerks and of the plantar reflexes persisted; and up to the present time (June, 1914) severe sensory loss still exists in both lower extremities, greater to pain, heat and cold on the right side and to posture, vibration and tactile discrimination on the left. He has never regained full control over his sphincters.

On January 29, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.-.}{\text{cs.f. } 4.4.4.0.0.}$ and the cells numbered 1 per cubic millimetre.

On June 10, 1914, the Wassermann reaction was $\frac{\text{serum } 4.4.4.4.0.}{\text{cs.f. } 3.0.0.0.0.}$ and the the cells numbered 1 per cubic millimetre.

He now walks with much greater security, but the physical signs of nervous disease remain unchanged.

We could give other instances of these mixed forms where the disease attacks meninges, vessels, and deep structures simultaneously; but we have selected these three examples because of the diversity of their clinical symptoms and because they had all been subjected to unusually energetic treatment, more than sufficient to cause a profound change in the Wassermann reaction of the cerebrospinal fluid, had they been instances of uncomplicated meningo-vascular syphilis.

Thus we believe there are cases where the spirochætes affect directly all the various structures which go to make up the central nervous system, meninges, vessels, neuroglia, and nerve elements. Such patients may show considerable improvement under treatment, but the strength and character of the Wassermann reaction will either undergo no material alteration, or will change extremely slowly compared with an otherwise uncomplicated case of meningo-vascular syphilis. These are instances of combined meningo-vascular and central syphilis in the same patient.

## Chapter VII.—General Conclusions.

In previous chapters we have described the behaviour of the Wassermann reaction under the various clinical conditions produced by syphilis of the central nervous system. But before passing on to the final detailed summary of our results it will be well to review certain more general conclusions at which we have arrived.

The first lesson we have learnt is that clinical signs reveal the site of the lesion but not the nature of the process which has produced it. It is, in many cases, impossible by bedside examination, however careful, to determine whether the patient is suffering from dementia paralytica or syphilitic "encephalitis." Were both conditions of equally fatal prognostic import this question would be a purely academic one. But we have given examples to show that if the patient is suffering from the cerebral form of meningo-vascular syphilis he may be profoundly improved by treatment, whereas in dementia paralytica he is doomed to inevitable and progressive mental decay. Numbers of persons

suffering with cerebral syphilis are condemned to die untreated because they are thought to be suffering from "general paralysis," whereas in reality they are examples of a curable disease.

The treatment of syphilis by modern therapeutic measures is so expensive and troublesome that few inmates of our Asylums and Workhouse Infirmaries receive adequate injections of neosalvarsan or even effective mercurial treatment. No one wastes time and money on persons supposed to be obvious cases of "general paralysis," and we have received letters from medical officers in answer to our inquiries about some patient expressing wonder that we should "take so much trouble over such a straightforward case of general paralysis."

In the same way a single clinical examination fails to reveal the nature of a case of muscular atrophy, unless the pupils happen to be affected or some other sign is present pointing to its syphilitic origin. We cannot say whether the disease can be arrested, or even perhaps cured, until we have watched the effect of efficient treatment on the signs and symptoms and on the Wassermann reaction in the cerebrospinal fluid.

Again we have shown that "gastric crises" are not of necessity a sign of tabes dorsalis. Any subacute irritation of the fibres of the thoracic posterior roots, whether inside or outside the substance of the spinal cord, may lead to periodic attacks of uncontrollable vomiting. The diagnosis of tabes dorsalis has to be made, not on the character of these attacks or the changes in thoracic sensibility, but on the additional signs of disease in the posterior columns.

But even when we have reason to believe that the posterior columns of the spinal cord are affected as the result of syphilis, we cannot necessarily diagnose tabes dorsalis in every case. Interference with the functions of these columns is not always due to a systemic reaction but may be secondary to vascular changes such as occur habitually in syphilis meningo-vascularis. Treatment and observation of the behaviour of the Wassermann reaction in the cerebrospinal fluid alone will reveal whether we are dealing with changes in the posterior columns secondary to vascular disease or with that systemic reaction to the virus which forms the essential lesion in tabes dorsalis.

A second lesson to be learnt from this research is that the signs and symptoms of syphilis of the central nervous system do not of necessity differ in the various stages of the disease. Two patients may be attacked for the first time with identical nervous manifestations:

yet the one is obviously in the secondary stage, three months after infection, whilst the other was infected twenty-five years before. As far as syphilis of the nervous system is concerned, we have no occasion to speak of "secondary" or "tertiary" or "parasyphilitic" manifestations. The lesions of cerebrospinal syphilis are produced by the reaction of the meninges, the vessels, the neuroglia and the essential elements of the nervous system, to the activity of the *Spirochæta pallida*. The clinical picture expresses the situation of this tissue-reaction, and signs and symptoms will remain the same whenever identical structures are attacked.

Throughout this work we have attached much importance to the behaviour of the Wassermann reaction in the cerebrospinal fluid as the result of treatment. We have gone so far as to suggest that when this reaction can be changed from positive to negative within a few months the pathological changes are mainly in the meninges and vessels. On the other hand should the cerebrospinal fluid remain essentially unchanged in its reaction in spite of identical treatment, we believe that the virus is exercising its activity on parts remote from the direct influence of the blood-stream.

Such a hypothesis, however, depends on two purely empirical procedures. For firstly we have given no facts to show that more energetic treatment, even with neosalvarsan, would not convert a positive into a negative reaction in the same time. We are only justified in stating that the doses we have habitually administered (0·9 grm. of neosalvarsan intravenously) do not materially change the reaction within six months. Secondly, the Wassermann reaction is itself a purely empirical procedure and we do not yet know all the factors which lead to changes in its strength and character.

It is quite impossible to base any pathological theory on the changes produced in this empirical reaction by a purely arbitrary therapeutic procedure. A new reaction or a new drug may change all our conclusions. Our work has simply established the fact that in certain cases of syphilis of the central nervous system, a definite dosage of one drug will so change the character of the cerebrospinal fluid that it will either give a negative Wassermann reaction or one greatly reduced in positive strength.

We do not suppose that there is any difference in principle, pathologically, between the cases which can be influenced and those which cannot; in certain doses the drug we have employed can reach the site

of the activity of the virus in one case, whilst in the other it is materially ineffective. Our statements are therefore of diagnostic and prognostic value solely under the present conditions of therapeutics and with the serological methods we have employed. We have established what these methods can do, but in no way suggest an essential pathological difference between the two classes. Nor do we believe that any line can be drawn scientifically between the two conditions. Sometimes the virus is acting mainly on the connective tissues and vessels, sometimes on the neuroglia and essential nerve-structures; but in many instances its activity must be widely distributed. At present our power of changing the character of the Wassermann reaction in the cerebrospinal fluid and of materially influencing the disease within a comparatively short period is confined to the cases where the lesion is mainly meningo-vascular. But a new drug, capable of penetrating to the essential structures of the nervous system, may render syphilis centralis amenable to treatment, and our categories will at once cease to have their present value.

The character of the Wassermann reaction in the cerebrospinal fluid can be profoundly influenced in many cases by suitable treatment, and the general condition of the patient may be greatly improved. But whenever syphilis has been active in the central nervous system for any considerable period, the phenomena of which the patient complains still persist to a greater or less extent. This disappointing result is due to the secondary changes which must occur in the structure of the nervous system in consequence of the mechanical effects of the syphilitic lesions. The patient is left with some permanent destruction in almost every case. A man remains characteristically tabetic although the morbid process has apparently died out (No. 83, p. 102). Primary optic atrophy or amyotrophy may remain unchanged although the Wassermann reaction has become negative in both serum and cerebrospinal fluid. In the same way a residual dementia may be left after an attack of so-called "encephalitis" has passed away (No. 59, p. 37). Even gastric crises are not necessarily brought to an end by the apparent cessation of the active syphilitic process (No. 147, p. 22).

When once a portion of the central nervous system, such as the optic nerve or the long tracts in the posterior columns, has been destroyed we should not expect the functions performed by these structures to be restored. The patient remains blind or ataxic. Moreover this research has taught us that paroxysmal manifestations are not

necessarily produced by acute disease. Recurrent pains and paroxysmal vomiting do not necessarily cease because clinical observation and the Wassermann reaction in the cerebrospinal fluid show that the disease is no longer active. Throughout our work we have found many examples of the law, little recognized by neurologists, that a stationary disease may produce paroxysmal manifestations.

If these secondary changes are to be avoided, the diagnosis of cerebrospinal syphilis must be made early in the course of the disease; we must not wait until a man has become spastic or hemiplegic or shows profound muscular wasting before recognizing that the virus is active in his central nervous system. The changes in character and aptitude, the headaches, malaise, attacks of shivering, neurasthenic symptoms and the early manifestations described in Chapter III should at once arouse suspicion that the central nervous system is infected.

But of all the early symptoms changes in sensibility are among the most important; they demand, however, the most careful examination. The ordinary rough methods in unskilled hands are more liable to lead to confusion than to clearness of diagnosis. But when skilfully investigated, the over-reaction to unpleasant stimuli, the slight loss of sensation within areas of apparent hyperalgesia, the bands of changed sensibility, &c., form an important aid to early diagnosis. Moreover, these abnormal sensations disappear rapidly after efficient treatment, and usually leave no permanent disability behind them.

On looking through our records of these root-affections it is at once evident that some areas tend to appear more often than others, and we should like to suggest a possible reason for this fact. According to Orr and Rows [17] the perineural lymphatic space which surrounds every spinal nerve and extends along the roots to the pia mater is an afferent lymphatic channel of the cerebrospinal axis. Toxic material ascends by this system of lymph-spaces from the skin or other deep foci of infection to produce profound changes in the nervous system. On its path inwards through the spinal nerve-roots the poison is liable to produce in them an inflammatory reaction. Both Ehrmann and Levaditi have shown that the *Spirochæta pallida* may pass from a primary sore up the peripheral nerves, and it probably reaches the central nervous system by way of the spinal nerve-roots.

Now we find that the roots most commonly subjected to irritation are those in connexion, by their visceral afferent fibres, with certain organs known to be the seat of active spirochætosis in syphilis. Thus

the second and third cervical, as we know from referred pain, contain the afferent paths from the tonsil. Another common group of root-areas is the first, second, third, and fourth thoracic which contain the afferent paths from the aorta to the central nervous system. But of all the root-areas which appear in syphilis, those from the seventh thoracic to the first lumbar are the most frequent. These roots carry the afferent paths from the liver, kidney, suprarenal and testicle, organs above all others liable to be crowded with spirochætes.

Lastly, we come to the second, third and fourth sacral; the affection of these roots probably has a double origin, and is partly due to the frequency with which secondary syphilitic manifestations appear round the anus. Possibly, however, these roots become infected from the penis and urethra, with which they are intimately connected.

We believe that this infection usually occurs in the secondary period, but dies away rapidly under general treatment. Later, however, it is liable to blaze up again and produce those symptoms and signs of irritation of the posterior nerve-roots which we believe to be of such diagnostic importance.

## Summary.

(1) All manifestations of syphilis of the central nervous system are consequent on the direct activity of the *Spirochæta pallida*.

(2) The clinical picture evoked depends on the situation of this activity and on the susceptibility of the tissues.

(3) When the lesion lies mainly within the essential structures of the central nervous system both neuroglia and the nerve elements participate in the tissue-reaction. This results in the death and degeneration of certain systems of cells and fibres; to these secondary consequences may be due the greater part of the clinical manifestations [Chapter V, p. 86].

(4) The more closely clinical signs and symptoms point to pathological changes in the meninges and vessels, the more certainly will the disease yield to adequate treatment [Chapter IV, p. 84].

On the other hand, the more nearly the clinical manifestations point to one or more foci of syphilitic activity within the parenchymatous tissues of the central nervous system, the less will they yield to the present methods of anti-syphilitic treatment [Chapter V, p. 124].

(5) In syphilis meningo-vascularis the character of the Wassermann reaction in the cerebrospinal fluid depends upon whether the spinal or

basal meninges are affected. Should clinical evidence point to affection of the contents of the spinal canal, and occasionally when the basal meninges alone appear to be affected, the reaction is positive in the cerebrospinal fluid. When, however, the disease seems to be limited to the intracranial contents, the reaction in the cerebrospinal fluid tends to be negative or weakly positive [Chapter IV, p. 79].

(6) In cases of syphilis centralis, such as dementia paralytica, tabes dorsalis, muscular atrophy and primary optic atrophy, the Wassermann reaction in the cerebrospinal fluid is strongly positive so long as the disease is active. When, however, it has come to an end, leaving behind it a greater or less amount of irreparable degeneration, the Wassermann reaction may diminish in strength or even become negative in the cerebrospinal fluid [Chapter V, p. 101].

(7) Under treatment with salvarsan or neosalvarsan, the Wassermann reaction in cases of meningo-vascular syphilis, if at first positive, will usually become negative in the cerebrospinal fluid within six months [Chapter IV, p. 84].

On the other hand, the more the clinical manifestations point to syphilis centralis the less will they yield to any of the present forms of anti-syphilitic treatment [Chapter V, p. 124, and Chapter VI, p. 126].

(8) Thus no complete diagnosis or prognosis can be made until the patient has been under observation and treatment for at least six months, and the cerebrospinal fluid has been systematically examined from time to time.

(9) It is essential to employ a standard serological technique, such that the Wassermann reaction can be estimated quantitatively. The results given in this paper bear testimony to the uniformity and trustworthiness of the methods adopted by Dr. Fildes for performing the Wassermann reaction (Fildes and McIntosh [3]).

(10) Whatever the situation and nature of the lesion which is responsible for the clinical manifestations, some secondary degeneration must almost certainly result. Many of the signs and symptoms in cases of syphilitic disease of the central nervous system are therefore not amenable to any form of anti-syphilitic treatment.

(11) It is, therefore, most important to make the diagnosis of syphilis early in disease of the central nervous system, so that treatment may be employed before the advent of these secondary changes. In Chapter III we have considered a number of nervous conditions which are early manifestations of syphilitic disease (p. 7).

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# A COMPARISON OF THE LESIONS OF SYPHILIS AND "PARASYPHILIS," TOGETHER WITH EVIDENCE IN FAVOUR OF THE IDENTITY OF THESE TWO CONDITIONS.

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In a previous paper [22] we have published a short review of the evolution of opinion regarding the relation of "parasyphilis" to syphilis of the nervous system.

Originally, syphilis was not even considered to be an essential precursor of "parasyphilis," but gradually it became evident that without syphilis there was no "parasyphilis." This latter condition was looked upon as a non-syphilitic sequel of syphilis; a form of degeneration consequent upon syphilis, but not an active syphilitic inflammation due to the virus of the disease. On the other hand, more recently the opinion has been repeatedly expressed that "parasyphilis" is an active inflammatory process presumably due to the *Spirochæta pallida*, but differing from the ordinary manifestations of syphilis in some unknown particular. On the whole very little attention has been paid to such suggestions, since little effort was made to account for the admitted distinctions between syphilis and "parasyphilis" of the nervous system.

For the past three years, in collaboration with Dr. Head and Dr. Fearnsides, we have been engaged in a study of these questions, and our general conclusions have been shortly summarized already [23].

We expressed the view that "parasyphilitic" diseases are essentially syphilitic; that they are not degenerative sequelæ of syphilis, but are themselves active syphilitic processes due to the *Spirochæta pallida*; finally, that they are not syphilitic lesions of an unusual or particular form, but that they resemble in all essentials such lesions found elsewhere in the body.

In order to elaborate this view, we analyse in the following pages the exact type and nature of syphilitic lesions throughout the body generally, and then compare them with the essential lesions of "parasyphilis."

This paper is intended to be read in conjunction with our publication upon the Wassermann reaction [7], and also with that by Dr. Head and Dr. Fearnsides appearing in the present issue.

We desire to express our thanks to Professor Bulloch again for the continued interest he has taken in our work.

## Chapter I.—The Tissue Reaction in Syphilis.

### Introduction.

The variety of the lesions occurring in the course of syphilis, and the definite progression of the different stages are phenomena which have been well recognized since the earliest times.

It was known that the infection gave rise to a local sore, that the local sore was soon followed by a general exanthem, and finally, that

after a lapse of time sequelæ of a distinctive type might follow. The disease thus came to be divided into three periods often called "the period of local eruption," "the period of general eruption," and the "period of gummy deposits."

This classification has dominated the pathology of syphilis until the present day. The three periods were taken to represent definite stages in the progress of the disease, the local and general eruption and the gummy deposit being the characteristic features of these periods. In the period of local eruption the virus was thought to be entirely localized, while the general eruption marked the time of generalization. The gummy deposit, on the other hand, was looked upon as an entirely different type of lesion to those found in the first two stages, and, in fact, its dependence upon the virus of syphilis was often disputed.

In this manner has arisen the belief that the chancre, the cutaneous rash and the gumma are the characteristic manifestations of the three stages of syphilis, and that being characteristic they are capable of being readily distinguished one from another by pathological or clinical methods.

On investigation, however, it will be found that these lesions can only be described as "characteristic" in general terms. The primary sore, indeed, presents features very different from the lesions of the secondary stage, and similarly these latter may be readily differentiated from "tertiary" granulomata; but nevertheless it must be remembered that the macroscopic features by which these various lesions are recognized are frequently ill-developed, and it may then be difficult to determine the exact stages to which they belong.

An ulceration of the penis may be so "atypical" that the question may be debated as to whether it is a "primary sore" or a tertiary "pseudo-chancre," and similarly some of the cutaneous ulcerations of late secondary syphilis have so little in common with an ordinary secondary lesion that they may be looked upon as tertiary. Thus, although it may be admitted that the manifestations of syphilis in their most typical forms are characteristic for the various stages of the disease, nevertheless there is no definite particular in which one stage may be said to differ essentially from another.

Even in the microscopic anatomy the differentiation is no more precisely marked; it is often said that the occurrence of "endarteritis" or even a peculiar liability to necrosis is a feature of tertiary syphilis, but on critical analysis it is found that both "endarteritis" and necrosis are familiar features of all stages and are not characteristic only of the

tertiary period. They are merely present at this time in their most pronounced form. In fact, if in early examples the essentials of syphilitic lesions are studied, it will be found that they exhibit a general similarity, and that, as Virchow first pointed out, the appearances "characteristic" of the various stages are due to entirely secondary phenomena.

### The Comparative Histology of the so-called "Characteristic" Lesions of Syphilis.

If the histology of a primary sore be examined it is found to consist of a granuloma, the most marked features of which are perivascular collections of lymphocytes and plasma-cells, associated with a proliferation of the walls of the affected vessels. This proliferation may, indeed, lead to obliteration and thrombosis as a secondary phenomenon, and later an overgrowth of the connective tissue may produce a general fibrosis.

The cutaneous lesions of the secondary period are essentially similar and differ only in their greater acuteness. The capillaries are congested and their walls are proliferated, while surrounding the vessels are collections of lymphocytes and plasma-cells. In the more chronic affections an induration may be produced, as in the primary sore, by the overgrowth of fibroblasts.

Again, the tertiary lesion, the gumma, in favourable specimens may be observed to have its origin in a perivascular inflammation. The same proliferation of the vessel wall is manifest and the same accumulation of cells. The chief difference lies in the more pronounced secondary effects of the process. The cell accumulations are larger and more focal and the proliferation of the fibroblasts more marked. Thus the interruption in the blood supply and other factors determine an early degeneration and more marked necrosis in these foci.

The distribution of the *Spirochæta pallida* in these lesions is also very similar.

In the primary sore they are found in large numbers among the cells of the Malpighian layer and in the subcutaneous lymphatics. Further they are associated with the perivascular accumulations of cells, in the walls and actually in the lumen of the affected vessels. The same distribution occurs in the secondary lesion, although in this case the organisms are particularly concentrated upon the walls of the vessels rather than in the surrounding lymphatics.

In the gumma the relation of the spirochætes to the cellular histology is less well known, since in these lesions they are extremely

sparse. From an examination of the miliary gummata as found in the liver of a congenital syphilitic fœtus, it is seen that the organisms are in the proliferated walls of the central vessel and a similar relation has been described in very early gummatous lesions of the adult. In most cases of acquired tertiary syphilis, however, the degenerative process is already so far advanced before the lesion comes under observation that spirochætes can seldom be demonstrated. Indeed it has been supposed by some that the virus is not present in such cases in the form of a spirochæte, but such suggestions are negatived by several well authenticated instances. It is undoubtedly true that very few organisms are found in tertiary lesions, as might be supposed from their trivial infectivity, and this fact constitutes one of the most striking differences between early and late syphilis. In the former, the lesions of the acute stage, the spirochætes are numerous; in the latter, the chronic manifestations, they are few in number.

From the foregoing account it will be seen that as regards the histology of the "characteristic" lesions there is no essential difference in the three stages. They all contain the *Spirochæta pallida*, and this organism represents the irritant about which the cell reaction is found. Nevertheless, the tertiary process undoubtedly differs from the primary and secondary in that it is caused by a very much smaller number of spirochætes. This difference may be looked upon as a qualitative difference, and the same may be observed in the cellular reactions. In all cases the lesion is found to consist of an infiltration of lymphocytes, plasma-cells, and, usually, fibroblasts. There is a great tendency to form accumulations in relation to blood-vessels and these accumulations are swollen by a proliferation of the actual walls of the vessels themselves.

Such differences as are found between the appearance of the lesions of syphilis in the mesoblastic tissues depend chiefly upon the acuteness or chronicity of the condition. The type of the constituent cells is the same, but the different varieties are present in different proportions and undergo different modes of resolution or degeneration.

## The Comparative Pathology of Syphilitic Lesions.

In the preceding section we have shown that the "characteristic" cell reaction to the *Spirochæta pallida* is very similar in both acute and chronic syphilis. It is, however, necessary to point out that we have only dealt with those cell reactions which have for long monopolized

attention, namely, the reactions of the mesoblastic tissues. The disease of syphilis is too often studied as a series of cutaneous manifestations. There is a tendency to look upon the secondary period as the period of the rash, or upon the tertiary as the period of ulceration of the skin. It must not be forgotten that syphilis is not a disease of the skin; it is a general infection which involves all parts of the body at all periods. The skin lesions are only remarkable in that they are the most obvious. Their importance is certainly secondary to the affections of the internal organs.

We will therefore compare the pathology of the "characteristic" lesions already described with that of the internal organs.

For this purpose it is only necessary to discuss two periods of syphilis; the acute, corresponding to the secondary, and the chronic or tertiary.

The term "primary period" is strictly a misnomer. There is no primary period from the pathological point of view. A lesion, indeed, usually occurs at the point of inoculation, but this lesion is merely an incident in the incubation period of the acute symptoms. Its occurrence is more or less accidental and, as is now well known, it is often absent.

It will be remembered that within a few hours after inoculation the spirochætes have already wandered into the regional lymphatics and that within a few days they may be detected in the blood and internal organs. The virus is therefore generalized long before the appearance of the primary sore and this lesion cannot be looked upon as denoting a "period of local eruption." Conveyed by the blood-stream the spirochætes may lodge in any internal organ, spreading through the capillary walls and wandering through the lymphatics into the essential parenchyma itself.

This invasion of the internal organs in the acute stage leads sometimes to symptoms of great gravity, but for the most part the effect is not severe. An invasion of the liver may cause jaundice, or a nephritis or orchitis may occur; on the other hand the intoxication of the organ may be excessive and lead to widespread destruction of the parenchyma. This effect upon the organs is not merely due to the effect of the virus upon the interstitial tissues, such as may be seen in the cutaneous lesions, giving rise to a perivascular proliferation and infiltration of small cells; it is due chiefly to a primary intoxication of the parenchyma itself.

The effect of the intoxication upon the two types of tissue, interstitial and parenchymatous, will apparently be different, although essentially

of the same nature. There will be a reaction to stimulus, and in this reaction some of the cells will succumb and degenerate. The difference between the interstitial tissues and the parenchyma is that in the former the reaction is marked—proliferation and infiltration—while the degeneration is slight, and in the latter the reaction is trivial and the degeneration extensive.

This result is due to the different functions of the two types of tissue. One of the activities of the interstitial tissue is to proliferate and combat, in a phagocytic sense, a microbic infection. The parenchyma, on the other hand, is devoted to some particular metabolic function; it is a specialized tissue which does not participate in a phagocytic reaction. It has only a limited power of repair or regeneration, and therefore if the intoxication exceeds a certain limit, degeneration will follow.

In this manner in the acute stage of syphilis lesions of the internal organs may occur, in which a varying degree of degeneration of the parenchyma is found. The extent of the destruction depends upon the extent to which the spirochætes migrate from the capillaries and lymph spaces.

As the acute stage of syphilis subsides, there is a general destruction of the spirochætes throughout the body, but as shown by the subsequent relapses the destruction is not complete. Isolated foci are left in those organs and parts of the body into which the destructive agents, whether drugs or natural antibodies, have not succeeded in penetrating. In these situations the spirochætes lie "dormant," but are capable of exacerbation, under circumstances which are not understood, and of producing tertiary lesions.

The "typical" tertiary lesion, as already described, is the gumma, but just as a papule is not the only secondary lesion, so the gumma is not the only result of the exacerbation of the *Spirochæta pallida*. A gumma is produced by a focus occurring in or about the wall of a small blood-vessel; it is a perivascular proliferation and infiltration of the interstitial tissues, and when occurring in an organ, the intoxication only affects the parenchyma in the immediate neighbourhood of the focal lesion. In tertiary syphilis, however, there are types of organ lesions which are sometimes referred to as "non-gummatous" or as diffuse infiltrations, leading to a diffuse fibrosis and destruction of the parenchyma. This type of lesion is comparable to the diffuse inflammations of the acute period. The intoxication is not focal as in the gumma, but diffuse, and, therefore, there is not only a diffuse reaction of the interstitial

tissues but a diffuse intoxication and resultant degeneration of the parenchyma.

It may be said, therefore, that the lesions of syphilis are similar both in the acute and chronic stages; in each the interstitial tissues and the parenchymatous tissues are involved. The affections are of two main types; the focal represented by the papule and the gumma, in which the virus is perivascular and exerts its effect chiefly upon the interstitial tissues; and the diffuse, in which the intoxication is diffuse and in which the effect, therefore, falls most obviously upon the parenchyma.

The ultimate result of these two varieties of lesion upon the integrity of the organ will be entirely different. The interstitial lesion need produce no notable symptoms and derange no important function; with suitable treatment it may entirely resolve. It is, however, quite different in the case of the parenchymatous lesions. As already described, if the intoxication proceeds beyond the narrow limit of repair, the cells will degenerate, and with them will be lost the special function of the organ. Under these circumstances the treatment, which was efficient in dealing with the interstitial lesion, will be without avail. The symptoms will be occasioned not by the presence of syphilis, but by the absence of the parenchymatous tissue. This loss of function, well illustrated by the sterility following a parenchymatous orchitis, is irreparable.

*Syphilitic lesions of the liver.*—The pathology of the lesions produced by syphilis in the internal organs may be illustrated by a consideration of the affections of the liver.

In this organ the extreme types of syphilitic inflammation are to be found in the "acute yellow atrophy" and the "solitary gumma." Both these conditions may be described as rare. The former has been recorded as occurring in the early secondary stage and is due to a diffuse dissemination of the virus throughout the organ. Microscopically, there is found a profound general degeneration of the liver-cells with little, if any, interstitial reaction, at most an infiltration of lymphocytes. The disease runs a rapid course and ends in death.

The gumma of the liver, on the other hand, is a purely local lesion, and originates in a reaction about a focus of spirochætes lying around a blood-vessel. The virus will produce about itself a reaction both of the parenchyma and also of the interstitial tissues, but since the destruction of the former will be purely local the result will not obtrude itself upon the microscopic picture. The interstitial reaction,

on the other hand, will consist of a local proliferation of the fixed cells and an accumulation of the wandering cells, and this focal reaction will result in a conspicuous granuloma. The liver-cells surrounding the focus will be separated by the infiltrating wandering cells, but this infiltration does not necessarily imply the presence of the spirochætes in its midst. The cells merely utilize the lymphatic spaces as channels by which to reach the virus, situated in the main focus of attraction. The tissues in which they lie are not directly affected by the spirochæte any more than the blood is affected in leucocytosis by the cocci in an abscess. Thus the main mass of liver-tissue proper surrounding a gummatous focus is more or less normal; only those cells in the immediate vicinity of the initial focus are destroyed.

In acute yellow atrophy, therefore, since the distribution of the virus is diffuse, the reaction and destruction is most marked in the parenchyma, while in the focal gumma the most obvious effect is upon the interstitial tissues.

The two extremes mentioned are, however, rare, and many intermediate types are found. The gummatous process, for instance, usually results from the fusion of a number of smaller foci and according as the virus is more or less diffused from these foci, the parenchyma is more or less involved in the process. Thus a diffuse reaction in the parenchyma may be associated with focal gumma formation in the same liver.

Certain examples of congenital syphilitic livers illustrate the mean between the two extreme types. In these cases the invasion from the portal vein results in a very large number of points of infection. The spirochætes lodge in the small vessels and multiply in their walls. From here they invade the surrounding lymphatics and even the liver-cells themselves. As a result a general reaction will take place both of the parenchyma and also of the interstitial tissues. The parenchymatous reaction is evidenced by duplication of the nuclei, and cell masses may be observed containing multiple nuclei and karyokinetic figures. This reaction of the parenchyma will usually end in a diffuse degeneration. The interstitial reaction is most marked about the infected vessels, and consists of an endothelial proliferation, while wandering lymphocytes fill the lymphatics between the liver-cells. The larger collections of cells tend to degenerate and form miliary gummata, while the more diffuse interstitial reaction leads to a diffused fibrosis of the organ. In such a case the incidence of the virus upon the two main types of tissues is relatively equal.

### Conclusions.

(1) The interstitial lesions of syphilis should not be looked upon as "characteristic" of syphilis to the exclusion of the parenchymatous. In addition to the interstitial reactions in the skin and internal organs, the essential parenchyma of these organs is also primarily involved in the intoxication.

(2) As a result of the stimulation by the virus the interstitial tissues will undergo a proliferation, but this will be absent or abortive in the case of the parenchyma. This tissue will usually degenerate, being incapable of extensive repair, and the secondary degeneration will entail a loss of function which will be unaffected by anti-syphilitic treatment.

(3) The above result is the effect of a diffuse dissemination of the virus, but if the spirochætes appear in a series of foci, the whole process will tend to take on a focal arrangement, and in this case the nodular interstitial reaction will tend to overshadow the local parenchymatous reaction.

## Chapter II.—The Factors governing the Amount of Tissue Reaction in Syphilis.

### Introduction.

In the preceding chapter we have shown that syphilis is a disease which affects not only the interstitial tissues at all periods but also the parenchyma of the internal organs and that the essential type of tissue reaction is the same at all stages of the disease. The difference between the appearances of a secondary and tertiary lesion, for instance, is due to secondary changes in the latter. These changes consist of excessive fibrosis and liability to degeneration. Further, we have shown that the number of spirochætes is large in a secondary lesion but small in a tertiary, and it thus follows that in these latter cases there is a remarkable lack of correlation between the amount of the virus and the extent of the lesion. In the secondary stage it requires a large number of spirochætes to produce a papule, while in the tertiary stage a large gumma may result from a number of spirochætes which is too small to detect. It therefore becomes necessary to inquire into the factors which govern the extent to which the tissues may react to the virus.

THEORIES ON THE RELATION OF THE VIRUS TO THE LESION.

At the present time every syphilitic lesion is looked upon as a response to the stimulus of the *Spirochæta pallida*. In former years, however, it was generally held that the tertiary lesions were not the direct effect of the virus and this view was supported by their notoriously slight infectivity. The discussion of the nature of the gummatous process was opened by Sir Jonathan Hutchinson [15] in 1866 as follows: "The occurrence of the tertiary symptoms is to be explained by the fact that during the exanthematic stage, when the whole blood was loaded with the virus, the various solids have received from that poisoned blood the elements necessary for their growth, and have been built up, so to speak, with syphilized plasma. Hence an impairment of organization in such tissues, and a liability under slight exciting causes . . . to the occurrence of specific forms of inflammation." Again, "The tertiary symptoms are not so properly a stage, but must count rather as the sequelæ, more or less accidental, of the preceding stages. They are as a rule not symmetrical, making it seem improbable that they depend upon blood taint. . . . From these facts we infer that they are due rather to the ill constitution of the affected structures than to any free virus still circulating in the blood."

It will be seen from the above quotations that the gumma was not looked upon as a syphilitic lesion in the sense that it was due directly to the virus of syphilis. Hutchinson considered that the syphilitic infection produced a state of body or diathesis in some ways akin to the scrofulous diathesis. This condition of the tissues ensured that any stimulus applied to them would produce the type of reaction known as a gumma.

In 1874 Bäumler [2] expressed very similar views. He looked upon the primary and secondary manifestations as the direct irritant result of the syphilitic virus affecting normal tissues, but "during the period of gummatous development it is probably no longer the action of the specific poison upon normal tissue with which we have to do, but with a sort of specific reaction of tissues, modified by previous blood-poisoning, under some accidental irritation."

Here, again, the gumma is looked upon as a specific lesion due to a non-specific cause, the specificity of the reaction being due to an alteration in the tissues induced by the previous infection.

So far as we are aware the first true recognition of the relation of the virus to the tertiary lesion is due to Eduard Lang [18]. In 1881 he stated that the virus of syphilis became disseminated throughout

the organs of the body at the time of the exanthem, but that subsequently the greater part was destroyed, "a remnant only lies latent in the tissues and this becomes manifest after any injury through the local production of new growths which are occasioned by the exacerbation of the virus, now essentially altered in character. The new growths represent the late forms of syphilis."

Lang further laid down the rule that "an organ which is the seat of a gummatous lesion must have been affected in the early period of syphilis."

It is thus clear that Lang differed from Hutchinson and the other syphilologists of the time in ascribing the tertiary lesion to the direct action of the virus, while the alteration in the appearance of these lesions was considered to be due to an alteration in the virus rather than in the tissues themselves.

Almost simultaneously Neisser [29] (1882) recognized the essential dependence of the gumma upon the activity of the virus. He, however, reverted to the theory of tissue alteration to account for the characters of the tertiary lesion, and referred to this alteration as an "Umstimmung der Gewebe," resulting from the action of the virus during the secondary period.

"This alteration in the tissues, soon after the infection, as soon as the disease has become constitutional, becomes an additional factor which has to be taken into account whenever the action of the virus itself is discussed. It certainly has nothing to do with a so-called anomaly of constitution (scrofulous, scorbutic, &c.), but is a specific alteration which the tissues undergo when they are themselves bathed in syphilis toxin."

Neisser was thus the first to look upon the tertiary process as an expression of the activity of the virus exerted upon tissues which had undergone a specific alteration after the acute period.

There can be but little doubt that the theory of tissue alteration propounded by Neisser, as opposed to the alteration in the virus suggested by Lang, is the correct explanation. It has been, however, frequently suggested that the different types of lesion associated with syphilis may be due to alterations in the virulence of the spirochæte, but while the possibility of such altered virulence must not be lost sight of, this view must be held to lack sufficient support.

When normal animals are inoculated with tertiary material, the resultant lesion is a typical primary sore with a relatively normal incubation period, and the primary lesion in the chimpanzee is

followed by a normal secondary stage. In some cases the incubation period is found to be prolonged, and this has been taken as evidence that the virus in tertiary syphilis is modified or attenuated. This may, indeed, be the case, but at the same time the prolonged incubation period may merely result from the small number of spirochætes in the inoculated material. A "tertiary" spirochæte, then, does not produce a "tertiary" lesion in a non-syphilitic individual, but a "primary" spirochæte will produce a "tertiary" lesion in a "tertiary" syphilitic (indurated pseudo-chancre, *vide* p. 155).

It is therefore clear that variation of the spirochæte has little bearing upon the differences in the appearance of syphilitic lesions at different stages. This is due to an alteration in the tissues produced by the previous activity of the infective agent.

### Allergie.

The nature of the alteration in the tissues was not further discussed until von Pirquet introduced his theory of "allergie" (1903).

This term "allergie" was not introduced in connection with syphilis, although von Pirquet [43] considered that this disease would afford a fruitful field for its study. The word was used to denote the alteration in the reactions produced by *second injections* of certain viruses. The original state studied was the "serum disease" produced in man by injections of horse serum, and later he studied vaccination and revaccination in the same light.

The alteration in the reaction following a second inoculation of a virus might be recognized in three ways: Firstly, by an alteration in the reaction *time*; secondly, by an alteration in the *extent* of the reaction; and, thirdly, by an alteration in its *quality*.

A classical example of allergie is found in Jennerian vaccination and revaccination.

Thus, where an individual is vaccinated for the first time, the full development of the pustule is observed on about the twelfth day; when, however, he has already been vaccinated a few months previously, and is then revaccinated, the lesion will attain its full development on the first day (alteration in the reaction time), but the characteristic features of the normal pustule will not develop (alteration in the reaction type), and the whole reaction will be smaller (alteration in the reaction extent).

The alterations in the reaction time are of two main types. Firstly, the immediate reaction ("sofortige Reaktion"), which is met

with when the "immunity" induced by the first injection is still present, and the quickened reaction ("beschleunigte Reaktion") occurring when several years have elapsed since the first injection and the "immune bodies" have disappeared from the serum. In revaccination the immediate reaction is observed when the second inoculation is carried out within about two years of the first; while the quickened reaction, i.e., a relative normal pustule with a shortened incubation period, occurs as a result of revaccination after a longer period.

The manifestation of allergie which most concerns the present subject is, however, the quantitative and qualitative alterations in the cell reaction. The lesion following a second inoculation may be smaller or larger than the primary lesion; in the former case the susceptibility of the tissues to the poison is depressed, and in the latter it is exalted. A well-known example of the latter state is von Pirquet's skin reaction in tuberculosis, when owing to the altered (hypersusceptible) state of the tissues induced by tuberculosis, an inoculation of a minute quantity of tuberculin will produce a large inflammatory lesion. The quality of the reaction will also differ from a primary tuberculous lesion, while the incubation period will be shortened to twenty-four hours.

Von Pirquet suggested that in all probability the manifold varieties of syphilitic lesions were also due to the state of allergie induced by the previous presence of the virus, and pointed out that Finger and Landsteiner had demonstrated a shortened incubation period after second inoculations of syphilitic material in monkeys, while inoculations in tertiary syphilitics produced an immediate ("sofortige") toxic erythema. This lesion he regarded as being due to a hypersusceptible state of the tissues produced originally by the *Spirocharta pallida* and as entirely analogous to the cutaneous reaction in tuberculosis. This view has more recently been accepted by Neisser [30], who stated that his "Umstimmung der Gewebe" was intended to imply an idea exactly similar to von Pirquet's allergie.

## Allergie in Syphilis.

In the following pages we enumerate various phenomena which occur in syphilis to illustrate the existence of allergie in this disease.

*Syphilization.*—Phenomena analogous to those following Jennerian vaccination may be observed in experimental syphilization, the two instances, however, differing, in that the former is a transient infection while the latter is chronic and persistent. As a result of a large number

of experiments on monkeys it has been demonstrated that second inoculations when carried out within a short period of the first (fifty-one days—Neisser) produce a second "primary lesion" with a shortened incubation period. This is a case of "Beschleunigung der Reaktion" due to an increased susceptibility of the tissues resulting from the first inoculation.

The tissues have become altered in such a way that they respond more readily to the stimulus of the virus. Similar results have been obtained by Pinard [42] on man. When, however, the reinoculation with syphilis is attempted in the secondary period, it is found that the virus is practically without effect. Very few instances have been recorded of lesions appearing as a result of reinoculation at this period, and it was only by the method of tissue implantation that Finger and Landsteiner, and Pinard succeeded in producing an insignificant papule. It is thus clear that in the secondary stage the tissues are very little susceptible to the *Spirochæta pallida*, although many of these organisms may have been present in the inoculated material. A change has taken place (allergie) in the direction of diminished susceptibility.

In the tertiary stage, however, the effect of reinoculation with syphilis is quite different. A lesion is produced after a very short incubation period, the so-called "sofortige Reaktion." The area involved is often of considerable size, and tissue destruction is so marked as to lead sometimes to ulceration. The effect of the inoculation is thus to produce a lesion of a "tertiary" character. This extensive reaction is not due to an excessive local growth of the spirochætes, since on examination these are seldom to be found; if they are discovered occasionally they are probably only the remnant of those injected.

Such a reaction is clearly comparable to the tuberculin reaction in tuberculosis. It is an abnormally great reaction of the tissues to the virus. The tissues have again undergone a change (allergie), but in this case in the direction of increased susceptibility. They have become hypersusceptible and, therefore, react in an excessive manner out of all proportion to the quantity of spirochætes injected.

Syphilization in tertiary syphilis is commonly observed as the "indurated pseudo-chancre." This is an ulcerative lesion of a "tertiary" character and very seldom contains the *Spirochæta pallida*. It is without doubt produced by the implantation of a new strain of spirochætes upon a tertiary syphilitic. Instead of a Hunterian chancre appearing after a long incubation period, the hypersusceptible tissues react quickly as a tertiary lesion. These lesions are not "chancres"

and should not be described as "reinfections." They are superinfections and their appearance is due to an alteration in the tissues; the inoculated spirochætes do not multiply and they produce no constitutional symptoms.

*Cutaneous reactions.*—Results very similar to those obtained by syphilization may follow the application of the luetin test of Noguchi [32 and 33]. This test consists of the percutaneous injection of dead *Spirochæta pallidæ* obtained from cultures and is thus directly comparable to the cutaneous test of von Pirquet in tuberculosis. As a measure of allergie this test is less complex than is syphilization, since the effect is not obscured by the production or absence of the disease syphilis as a result of the inoculation.

We have found that in the later primary stage a slight positive reaction may usually be obtained, demonstrating an increased susceptibility in the tissues. During the secondary period, however, no effect is produced, since the tissues are not susceptible. In the tertiary period, on the other hand, the positive reaction is often very marked as a widespread inflammatory lesion. In non-syphilitic persons the inoculation produces no effect, although it must be admitted that as a diagnostic measure the test cannot be looked upon as being specific. By this method, therefore, it may be seen that a quantity of dead virus, which in itself is non-toxic, is capable of producing a lesion in syphilis at certain periods, these periods being marked by a condition of increased susceptibility to this virus. If in normal tissues a certain quantity of virus is capable of producing no effect, in hypersusceptible tissues the same quantity may produce a great effect.

*Allergie observed during the progress of the syphilitic infection.*—In the previous sections, we have described the state of allergie in the various stages of syphilis as demonstrated by reinoculations of syphilitic material, but a similar phenomenon may be observed in the actual manifestations of the disease.

Syphilis should be looked upon as exhibiting two periods only, namely, the acute, corresponding to the secondary, and the chronic or tertiary. For the purposes of simplification the primary stage so called may be omitted, since in fact it is merely an incident in the incubation period of the acute symptoms.

Both the acute and chronic lesions are reactions against a local toxin derived from the *Spirochæta pallida*, and the variable type of reaction (allergie) depends upon the different states of the tissues induced by this organism. At the time of infection the tissues are prac-

tically insusceptible to the *Spirochæta pallida*, and therefore no immediate reaction occurs. The local growth and rapid generalization of the virus, however, produces such an effect upon the tissues that they become more susceptible and thus develop an immunity reaction against the virus. This reaction is both "cellular" and "humoral," that is to say the tissues not only become more prone to a cellular reaction but also produce antibodies. The period of time which elapses before the immunity response has developed corresponds to the incubation period of the acute manifestations. The production of antibodies in protozoal diseases is often "critical," and thus in syphilis a "critical" output of antibodies occurs and leads to a "critical" destruction of a large number of spirochætes, and the consequent liberation of large quantities of toxins. These toxins will affect the sensitized tissues and create a generalized reaction or acute rash. The exanthem may thus be looked upon as representing a reaction to a dose of syphilis toxin in tissues which have undergone a certain degree of sensitization. These are more susceptible to the virus than they were before infection took place.

Following the rash, however, as has already been shown, the tissues have lost their susceptibility in that at this time an inoculation of the virus will produce practically no effect. This result is probably due to the phenomenon of "desensitization." It is known that when an animal has been rendered hypersusceptible to serum, for instance, this hypersusceptibility may be abolished under certain conditions by the reintroduction of the antigen (serum). Similarly the susceptible cells in syphilis may be rendered insusceptible by the general liberation of antigen (spirochæte toxin) at the time of the secondary rash. In the phraseology of Ehrlich it may be said that the avidity of the cell receptors is entirely satisfied by the virus and no excess of avidity (susceptibility) is left.

In this condition the cells in the manner of von Pirquet may be described as being "anergic," and it is in consequence of this anergie that the manifestations gradually disappear after the period of the exanthem.

During the "latent period," the virus is still retained in the body, producing an effect, outwardly at least, inappreciable, or in an entirely dormant state. At this time an increased susceptibility gradually develops in the tissues. The degree of susceptibility is much greater than that present in the early stage of the disease and thus, on exacerbation of the spirochætes, a lesion will be produced which is larger than a "secondary" tissue reaction, and which will show an alteration

in type leading to excessive degenerative changes (hyperallergie, hypersusceptibility). The alteration in the incubation period, on which great stress is laid by von Pirquet, cannot be demonstrated in the spontaneous tertiary lesion, since the actual time of exacerbation cannot be determined. In those cases, however, in which the tertiary lesion is produced by a foreign strain, that is, when an "indurated pseudo-chancre" follows from a superinfection in a tertiary syphilitic, it may be observed clearly that the incubation period is very much shortened, being reduced from one month, as in the primary period, to at most a few days ("Beschleunigung der Reaktion").

The alteration in the reaction of the tissues (allergie) is particularly obvious when attention is paid to the actual number of spirochætes giving rise to the various lesions. In the secondary stage, although the reaction is less, the number of spirochætes in the lesions is large, while in the tertiary lesions, even when of large size, the number of spirochætes is small; in fact in practice it is extremely difficult to demonstrate them in such lesions.

The reaction of the tissues in chronic syphilis has not only undergone a change in its extent, but the character of the cells is also different. As has already been pointed out, the initial lesion is the same in all forms of syphilis, but in chronic syphilis the secondary changes tend toward fibrosis and degeneration. This excessive degeneration is due to the hypersusceptibility of the cells. Although the hypersusceptible state is an immunity process designed as a protective mechanism by which the whole of the antimicrobic forces are rapidly brought into play, nevertheless the increased avidity of the cell receptors leads to an intoxication of the cells which is often excessive. Thus the tissues are not only more easily thrown into activity but are also more readily injured. The degeneration consequent upon this injury is the cause of the most "characteristic" features of tertiary syphilis, namely, the necrosis of gummatous tissue.

So long as the degeneration is confined to the interstitial tissues, the site of a gumma, no serious incapacitation of the patient need follow, but when a vital organ, and particularly the parenchyma of such an organ, is involved, the result is more important. If these cells have been rendered hypersusceptible and are then exposed to the action of the virus, they will usually be intoxicated beyond the limit of repair and will undergo a progressive degeneration which will entail a complete and irreparable loss of function of the organ.

The factors which determine the occurrence of the hyperallergic

reaction in syphilis are twofold, namely, the existence of the hypersusceptible state and the development of an exacerbation of spirochætes.

The state of hypersusceptibility is produced, as already stated, as an immunity reaction to the operation of the virus at a previous date. When present the condition will persist under favourable circumstances for years. It is known experimentally from the result of "luetin" tests that a certain degree of susceptibility develops before the onset of the acute rash, and this is no doubt due to the gradual multiplication of the virus in the tissues after infection. At the time of the rash, however, a large quantity of toxin is liberated, and this will result in a desensitization and insusceptibility which is characteristic of the secondary period following the exanthem. The liberated flood of toxin will, however, also act as an "antigen." The desensitization may be looked upon as a "negative phase," but after this has passed the state of susceptibility will reappear as the positive phase and will reach a height considerably above that present when the flood of antigen was liberated. The affected tissues will now be hypersusceptible and, in the absence of any process which might counteract this condition, will remain so for years. It is therefore clear that this state, which is found in the tertiary period, is directly due to an intoxication occurring at the time of the acute exanthem.

The second essential in the production of the hyperallergic reaction is the presence of the virus. All tissues within the body may be hypersusceptible, but no lesion will occur unless an exacerbation of the virus occurs to originate it. Some difference of opinion exists as to the source of this virus which actuates the tertiary lesion. On the one hand, the spirochætes may have remained locally in a dormant condition for many years, or perhaps they may have been "attracted" from a distant focus to an area of least resistance. It is known that certain parts of the body offer a suitable nidus for harbouring the spirochætes for many years, and it is possible that such foci are the source of those spirochætes which cause an exacerbation and produce a gumma at the site of some injury. Turnbull and one of us (P. F.) in a purely random selection of 314 *post-mortem* cases (not yet published) have found a very high incidence of syphilis in the aorta, this in many cases being the only syphilitic lesion demonstrable, and it is possible that such a focus may provide the spirochætes for gummatous processes in the skin or elsewhere. Mott has also recognized the high incidence of aortitis in asylum patients and has assumed that there is a direct causal connexion between aortitis and "parasyphilis," but from our results it is clear that

aortitis is as common, or even more common, when there is not only no "parasyphilis" but not even a syphilitic affection of the nervous system.

On the whole it is more probable that in most cases the site of exacerbation is governed by the accidental localization of the virus. The spirochætes are diffusely disseminated in the acute period and although the great majority are subsequently destroyed large numbers will remain secluded from toxic influences in relatively non-vascular areas and the walls of small vessels. These remnants will be diffusely scattered, and thus any part of the body may be the site of a spontaneous or traumatic exacerbation. Particular sites of predilection may exist, but on the other hand the frequency of lesions in particular organs may merely be due to particular strains and stresses to which these organs are exposed.

It would appear, therefore, that the hyperallergic reaction is due to two causes. Firstly, a sensitization of the area involved by toxins liberated in the acute period, and secondly, an exacerbation of spirochætes which have survived as "rests" from the general dissemination of the acute stage of syphilis. The cause of the exacerbation is unknown, but it is no doubt due to a local derangement of the balance between dormant virus and tissues. This derangement may be traumatic or may result from more subtle causes.

*The Wassermann reaction.*— Hypersusceptibility of the cells (hyperallergie) is not the only clinical manifestation of hypersusceptibility in syphilis; the same phenomenon may be observed in the Wassermann reaction. This reaction is, no doubt, dependent upon the degeneration of cells when specifically injured by the *Spirocharta pallida*, and it will therefore be some index of the amount of cellular destruction induced by this organism. Presuming then that a unit of "spirochæte toxin" produces relatively the same amount of cell destruction, it follows that the amount of cell destruction as evidenced by the Wassermann reaction will be proportional to the amount of "syphilis toxin" in operation. There is little reason to suppose that different strains of *Spirocharta pallida* vary largely in virulence; and therefore it is reasonable to believe that the strength of the Wassermann reaction is proportional to the number of spirochætes in the body.

This rule, however, only applies to early syphilis. During the first stages of the infection when the cells are insusceptible to the action of the toxin, no damage is produced and thus the reaction will be negative. But when, after a few weeks the susceptibility of the cells begins to

develop, an increasing number will be destroyed and thus the reaction will gradually gain in strength. The extensive lesion at the time of the rash will then account for the marked exacerbation of the Wassermann reaction which is often observed. From that time onward the spirochætes rapidly or slowly die out and the Wassermann reaction diminishes in proportion. In the latent stages a few spirochætes will be left and will produce an inappreciable lesion which may account for a slight positive reaction, or on the other hand a relatively extensive but undiagnosed internal lesion may exist together with a stronger reaction. In chronic syphilis, however, this correlation between the number of spirochætes and the strength of the reaction is absent. As is known at this time, there are very few spirochætes present, but nevertheless the Wassermann reaction is very strong, certainly as strong as it is in secondary syphilis. This lack of proportion is clearly due to the hypersusceptibility of the tissues, which leads to a great tissue destruction by a few spirochætes. This tissue destruction will occasion a strong Wassermann reaction, and thus in the tertiary stage the strength of the reaction will not be proportionate to the number of spirochætes causing it, although its presence will still indicate the effective activity of this organism.

## Conclusions.

(1) The fact that relatively little cell reaction is produced by a large number of spirochætes in acute syphilis, and an extensive reaction by a small quantity of virus in chronic syphilis, is due to an alteration in the susceptibility of the tissues to the virus. The alteration corresponds to that described by von Pirquet as "allergie."

(2) The phenomena following experimental syphilization, the result of cutaneous reactions and the manifestations of syphilis itself, are all explicable on the grounds of allergie.

(3) The type of allergie, hypersusceptibility, present in tertiary syphilis is developed as an immunity response to an intoxication of the tissues occurring in the acute stage of syphilis, and the actual occurrence of the lesion is due to an exacerbation of spirochætes which have remained dormant as a "rest" from the general dissemination in the acute stage.

(4) Although an immunity response, the state of hypersusceptibility leaves the tissues abnormally susceptible to the toxic action of the virus and thus the tertiary lesion is characterized by an excessive liability to degeneration.

(5) The most important sequelæ of these degenerations are to be found in the various organs. If the interstitial tissues are the site of the lesion, the type of reaction and degeneration known as a gumma will result. This reaction is not vital and is capable of undergoing repair. If the parenchyma is involved the abortive reaction will lead to a progressive degeneration, progressive because these tissues are capable of little repair. This degeneration will lead to the functional destruction of the organ, and such a result may be occasioned even by a small quantity of virus.

## Chapter III.—The Tissue Reaction in Syphilis and "Parasyphilis" of the Central Nervous System.

### Introduction.

Before describing the affections of the central nervous system it will be necessary to point out that we look upon the brain and spinal cord not as a "nervous system" but as one *organ* whose function is the correlation and transmission of nervous impulses. Together they correspond with the liver, kidney and other internal organs in that they are composed of a parenchyma and interstitial tissue. The parenchyma is represented by the proper nervous substance, while the interstitial tissue is of two varieties, the neuroglia and the mesoblastic interstitial tissue which is developmentally associated with the vascular structures.

### The Comparative Histology of the Syphilitic and "Parasyphilitic" Lesions of the Nervous System.

In reviewing shortly the lesions of syphilis as found in these organs, namely, the brain and spinal cord, it will be convenient to follow the classification already adopted in the preceding chapters dealing with syphilis generally. The "parasyphilitic" conditions will, however, be considered separately.

The central nervous system may be described as exhibiting three types of lesions: firstly, the acute lesions of the secondary period; secondly, the chronic lesions of the tertiary; and lastly, the "parasyphilitic."

#### *Lesions of the Secondary Period.*

It has, of course, been long recognized that palsies of the cranial nerves may result from inflammatory processes involving the meninges

or bony canals during the later secondary period. Particular attention has, however, been focussed upon these occurrences since the introduction of salvarsan. It has been alleged that treatment by this drug has introduced a greater incidence of nerve lesions than was the case formerly with mercury. Very extensive investigations have been directed to this point and, although the matter may still be considered *sub judice*, the general trend of evidence undoubtedly disputes the assertion. If an apparent increase in these so-called "nerve relapses" is observed, it is in our opinion largely due to two causes. Firstly, syphilis and its treatment is now the concern of a much larger group of observers representing much wider aspects of pathology than was recently the case, and thus unusual phenomena become the subjects of discussion when formerly they excited little comment. Secondly, the salvarsan preparations are remedies so much more potent than mercury that the ordinary cutaneous relapses have become infrequent and thus such incidents as the "nerve relapses," which may be less influenced by salvarsan, become relatively more conspicuous.

In this place, however, we do not propose to enter into a discussion of this question, but to confine ourselves to the nervous affections in acute secondary syphilis, while we regard the nerve relapse, whether following salvarsan or mercury or neither, as a later manifestation of secondary syphilis.

The occurrence of a meningeal lesion at the time of the general dissemination of the virus was first insisted upon by Eduard Lang [17] in 1880. He called attention to the headaches, lassitude and even torpor which often accompany the exanthem, and ascribed these to a meningeal "irritation" which in rarer cases might even become an infiltration or definite syphilitic meningitis. In certain fatal cases of syphilitic cerebrospinal meningitis, including that recorded in 1860 by Griesinger [12], he described the lack of correlation between the extent of the lesions found *post mortem* and the severity of the symptoms during life, and argued that a definite organic meningitis was common in acute secondary syphilis, although the manifestations produced might be trivial.

To judge from the literature appearing subsequently to Lang's account, the meningitis of secondary syphilis has not attracted very general attention and, in fact, some monographs dealing with syphilis of the central nervous system omit all mention of it. The cause of this neglect probably lies in the fact that the symptoms are usually trivial and amenable to treatment and thus autopsies are rare. On the other

hand, a patient may die with acute cerebral symptoms and the connection between these symptoms and syphilis may not be recognized. At the autopsy an œdema of the brain may be noticed and histologically an infiltration of the meninges, but such a lesion need not necessarily suggest syphilis, and even if it does, there will be no conclusive proof available. At the present time, however, the nature of such diseases is made apparent by the Wassermann reaction. The enormous bearing of syphilis upon neurology tends to require the performance of this test as a routine, while the operation of lumbar puncture is of almost daily occurrence in any neurological clinic. These methods may at once disclose the syphilitic nature of an acute cerebral condition, and if the patient dies the pathologist in his search for the cause is assisted by this previous knowledge.

In recent years as a result of the more general application of the operation of lumbar puncture, attention has again been focussed upon the early syphilitic lesions of the central nervous system. Thus Ravaut [45] (1903) examined the cerebrospinal fluid of a large number of acute syphilitics, and although no obvious nervous manifestations were present, nevertheless there was evidence of "meningeal irritation" in no less than 71 out of 118 fluids examined. Similar results have since been obtained by many, but notably by Altmann and Dreyfus [1] and Fraenkel [10]. In such cases the cerebrospinal fluid may be under increased tension, may contain an abnormal quantity of albumen or, which is most striking, may show a definite lymphocytosis.

Although there has been considerable discussion as to the precise explanation of these findings, there can be but little doubt in the light of subsequent knowledge that the lymphocytosis and adjuvant phenomena are an indication of "meningeal irritation," or in more accepted pathological phraseology of "meningitis." There is reason to believe that at the time of the generalization of the virus in the early stages of syphilis the serous membranes may be affected in the same way as the mucous membranes or skin, and according to Ellis [6] such affections may be present even before the appearance of the cutaneous exanthem. Several instances of this condition are recorded in the series of Dr. Head and Dr. Fearnsides. In particular we may refer to Case No. 313.[1] This female patient had acute secondary syphilis, and was observed in the fourth month after infection. No obvious nervous signs were present, but nevertheless there was a very marked pleocytosis in the

[1] For an account of this case *vide Brain*, 1914, vol. xxxvii. p. 30.

cerebrospinal fluid and also a positive Wassermann reaction. We have stated that no obvious nervous signs were present, but by the special methods of Dr. Head and Dr. Fearnsides distinct evidence of "root irritation" was obtained. In fact this patient in the early secondary stage had a marked meningitis of the spinal cord, and yet the only clinical evidences of this were a series of segmental areas showing cutaneous hyperæsthesia. We are of opinion that if a precise neurological examination of secondary syphilitic patients was made as a routine, clinical evidence of meningitis would be obtained in the majority of those patients who show pathological changes in the cerebrospinal fluid.

The relation of this meningitis to syphilis has been demonstrated by Hoffmann [13]. In a case of acute syphilis without obvious nervous manifestations he was able to demonstrate by inoculation of the cerebrospinal fluid into animals the presence of the specific virus, and thus, although in the absence of an autopsy the exact relation of the *Spirochæta pallida* to the meningeal lesion must remain somewhat conjectural, it is clear that the meningitis is an active process actually due to this organism.

In a few cases in which nervous manifestations developed somewhat later in the secondary period the presence of the *Spirochæta pallida* in the tissues of the nervous system has also been demonstrated. Gaucher, Paris and Merle [11] investigated a fatal case of hemiplegia developing seven months after infection. Perivenous collections of cells were found in the meninges of the spinal cord, and a proliferation of the endothelium of the vessels. The brain was œdematous and the meninges infiltrated. No spirochætes could be found in sections, although one was discovered in the cerebrospinal fluid. Nichols and Hough [31] also found spirochætes by inoculating into rabbits the cerebrospinal fluid from a case of hemiplegia nine months after infection, while in a similar type of case Sézary and Paillard [48] found spirochætes in the cerebrospinal fluid by the method of dark-ground illumination. Although the histology of the early secondary meningitis of adults must be described as being unknown, nevertheless it is probable that it bears some resemblance to the lesions found in infantile meningitis. Ravaut and Ponselle [46] examined a case of acute syphilitic encephalitis in an infant, and found the spirochætes situated in perivenous cellular collections. Ranke [44] also examined an infant and found large numbers of spirochætes in the lymphatics surrounding the vessels in the meninges and spreading out from the intima. A small

number of the organisms had also wandered from the neighbourhood of the vessels into the cerebral substance.

In further support of the suggestion that the nervous system is frequently involved in early syphilis, it will be permissible to refer to the researches of Steiner [50] and Jakob and Weygandt [16] upon rabbit syphilis. It will be remembered that syphilis in these animals tends to remain local and to progress towards spontaneous cure without obvious general symptoms. An infected rabbit may therefore be compared with a human being in the primary stage. Nevertheless the work of these authors shows that inflammatory lesions of the roots of the spinal nerves are constant, and even slight affections of the spinal cord and brain itself.

*Lesions of the Tertiary Period.*

Little difficulty is found in analysing the tissue reactions in the condition usually termed "gummatous meningitis." This is a lesion which affects the membranes of the central nervous system and also the prolongations of these membranes into the substance of the brain and cord. The term meningitis is therefore to some extent a misnomer, since the lesion may only affect the interior of the brain, while the actual coverings escape.

The gummatous process does not differ in origin from gummatous processes elsewhere. It is a granuloma forming about a small vessel, and by the confluence of a number of such foci the affected parts may be much thickened. The granuloma is formed by a proliferation of the fixed interstitial cells and an accumulation of wandering lymphocytes and plasma-cells, which may be observed in the surrounding lymphatics. The characteristic secondary changes, fibrosis and degeneration also follow.

The site of origin of the process is in the vascular tissues, and often in the walls of the cerebral vessels. The perivascular accumulations and the proliferation of the endothelium often lead to a thrombosis of these vessels, and thus the condition is sometimes referred to as "vascular syphilis"; the gummatous processes, however, in the body generally are no less "vascular" than those in the brain. Although the lesion may be widespread and involve not only the coverings of the central nervous system, but also the interior of these organs, nevertheless it appears to be confined to the lymph-vascular structures, and the nerve tissue proper is not grossly affected. Such lesions as are sometimes found may be due to a slight diffusion of the intoxication

similar to that which occurs in the parenchyma elsewhere about a gummatous process, or they may be merely due to pressure from exudates rather than a primary intoxication by the virus.

The relation of the *Spirochæta pallida* to the lesions of gummatous meningitis has been established in one case by Versé [53]. Small multiple gummata, in which central caseation was only just starting, were found in the meninges and the spirochætes were observed in the periphery of these nodules.

Among the so-called "gummatous" lesions of the brain are usually included those cases which really belong to the late secondary period and are not strictly "gummatous" at all. Thus in the case recorded by Strasmann [51] there was no gummatous process but a diffuse meningitis of the base and convexity of the brain. Large numbers of spirochætes were found in the walls and adventitial sheaths of the small vessels, which themselves exhibited endarteritis. The organisms were also found free in the meninges. The onset of the condition occurred two years after infection.

### "*Parasyphilitic*" *Lesions.*

*Dementia paralytica.*—If we confine ourselves to the essential alterations found in early stages of dementia paralytica, we find relatively simple lesions. The pia is in a state of inflammation, thickened and unduly attached to the underlying cortex. It may be infiltrated by large numbers of lymphocytes and plasma-cells, while the fixed elements including the endothelium of the capillaries and small vessels show a slight degree of proliferation. These cells, occupying the lymph spaces of the pia, also invade and inject the adventitial sheaths of the vessels which perforate the cortex at right angles, and thus in sections these vessels are clearly marked out not only by the proliferation of the connective tissue in their walls, but also by the passive infiltration by lymphocytes and plasma-cells.

In addition to these alterations of the mesoblastic elements of the brain, changes are also marked in the ectoblastic nervous tissue and the neuroglia. The injury to the ganglion cells is particularly marked; many may be observed to be swollen, while others exhibit all stages of chromatolysis and degeneration; the number of neuroglial cells is much increased; they appear to be especially condensed in particular localities.

As is well known, the presence of the *Spirochæta pallida* in the brain in dementia paralytica has now been demonstrated by Noguchi

and Moore [36]. In their first account they were able to find the spirochætes in twelve out of seventy cases. The distribution was quite different to that noticed in the secondary and tertiary lesions, in that the spirochætes were never found in the membranes or about the vessels, but always in the substance of the brain, and sometimes in relation to the nerve-cells. No connexion was demonstrable between the position of the organisms and the distribution of the cellular infiltrations. In Noguchi's [34] second series of observations he obtained a larger number of positive results, namely, thirty-six in 130 cases. Marie, Levaditi, and Bankowski [24] have confirmed Noguchi and Moore's results. In two out of twenty-four brains examined they found spirochætes with a distribution similar to that described by Noguchi and Moore. In a subsequent publication, however [19], they also illustrated a case in which large numbers of spirochætes were present, not only within the lumen of the vessels, but also in the walls, and migrating into the surrounding nerve tissues. Marinesco and Minea [26] also described an abnormal distribution in their one positive case among twenty-six examined; the spirochætes were situated in the meninges only, and not in the brain substance; but this case was not represented to be pure dementia paralytica, but dementia resulting from syphilitic meningitis.

When Noguchi first undertook the examination of brains from cases of dementia paralytica, it was with the hope of establishing a connexion between the granules found in his cultures of *Spirochæta pallida* and similar structures present in Levaditi silver preparations, and therefore his first discovery of a single typical spirochæte was unexpected. In some Levaditi preparations, as also with the modification introduced by Noguchi, the black granules are so numerous and are so often fortuitously arranged in a linear distribution that a connection between them and the *Spirochæta pallida* is still sometimes suggested. It is therefore of importance that this organism has been demonstrated by Noguchi, Levaditi, and others by the dark-ground method, and also in stained and unstained films. If any doubt remained that the spirochæte is present in the brain in no other than its ordinary form, this should be removed by the demonstration by Forster and Tomaszewski [9] and Berger [3] of typical living *Spirochæta pallida* in material obtained by brain puncture during life.

The identity of the spirochæte found in dementia paralytica with *Spirochæta pallida* has been proved by Noguchi [35] by means of animal inoculation. He was successful in obtaining testicular lesions in the

rabbit with brain substance from one out of six cases of dementia paralytica. The lesions were of slow onset, and contained few spirochætes, but these were quite typical. Uhlenhuth and Mulzer [52] have also obtained one positive inoculation in five, while Berger [3] succeeded in producing very small testicular lesions containing *Spirochæta pallida* in three cases out of twenty. There is no doubt that the long incubation period of the experimental lesion and its ill-developed character is abnormal when compared with the results obtained with acute syphilitic material; but, on the other hand, inoculation of tertiary products produce very similar effects. The abnormality does not appear to us to warrant the assumption of a special strain of spirochætes in dementia paralytica. The chronicity of the lesion is due probably to the small number of spirochætes in the inoculated material, and, no doubt, a certain loss of virulence following the long parasitic sojourn in the body.

We ourselves have examined a series of brains for the purpose of demonstrating *Spirochæta pallida*, and also to determine the relation of this organism to the histological changes. The procedure was to examine the specimen by the dark-ground method, and then to remove a "positive" area for histological examination and silver impregnation. We are indebted to Dr. Gettings, of the West Riding Asylum, Wakefield, for the material. Among the twelve specimens examined five exhibited lesions other than those of dementia paralytica, and in these no spirochætes were found. The remaining seven were typical examples of this condition, and six times undoubted spirochætes were discoverable by the dark-ground method. When these seven cases had been fixed and stained by Noguchi's method, however, positive results were obtained in four only. These were the ones in which the organisms had been most numerous.

By the technique which we have employed, the demonstration of the *Spirochæta pallida* is not attended with undue labour, but when examining the silver sections it is desirable to search rapidly without great concentration, since the distribution of the spirochætes is relatively focal, and when one is found, others are nearly always detected in the same neighbourhood; indeed, one focus may contain so many spirochætes that they could not be overlooked, while the rest of the section is relatively free.

The organisms are practically always confined to the grey matter; indeed, we have only once detected a single example in the meninges. We have been unable to observe any constant relation to the nerve

elements or to the blood-vessels, as described by Marie, Levaditi, and Bankowski. Indeed, the distribution of the spirochætes has been quite diffuse as regards the histological features, and especially has not been confined to the area of infiltration.

All the cases examined by us had exhibited relatively acute manifestations before death, and the brains themselves were not markedly wasted. The lesions appeared to be, on the whole, recent. Unfortunately, no "history" was obtainable in any case, and therefore the duration of the infection is unknown.

*Tabes.*—The histopathology of tabes dorsalis cannot be said to be clearly defined. In the case of dementia paralytica there is little or no dispute as to the actual lesions present, but in tabes, on the other hand, many lesions have been described as being present which are not generally accepted as characteristic. In many cases an isolated phenomenon is assumed to be constant, while, in fact, it has been inconstant or accidental.

The indefinite and contradictory nature of these reports is due to the fact that tabes dorsalis is a chronic disease, and the findings at autopsies in cases of all stages of development have been evaluated equally as bearing upon the essential lesions. It is quite clear, however, that the appearances seen in an advanced case of tabes dorsalis will be of little assistance in arriving at the essential nature of the process. The picture will be entirely confused by secondary inflammatory and degenerative changes.

With the growing knowledge that the etiology of general paralysis and tabes dorsalis was the same, it began to be recognized that the two conditions were neither clinically nor pathologically distinct.

Numerous cases were differentiated in which the symptoms of both diseases were present, and, *post mortem*, it was found that the lesions of tabes dorsalis were common in dementia paralytica. The great importance of this discovery lay in the fact that since the patients died early of dementia paralytica, the lesions of tabes dorsalis might be studied in their earliest forms before they had given rise to obvious symptoms. In our opinion a consideration of the essential pathology of the disease must be confined entirely to these early cases.

As is well known, the most obvious initial lesion of tabes dorsalis is a degeneration of certain exogenous nerve-fibres, situated in the posterior columns of the cord, and occupying the position known as the "bandelette externe." These fibres have their trophic centre in the posterior root ganglion, and form the central mass of the posterior

roots. The lesion tends to be symmetrical on both sides, although the process is more advanced in that first affected. In addition to these long fibres, others entering the cord from the posterior roots are affected. These are short fibres, which end in the grey matter of the cord. As the process advances, the confines of the degeneration enlarge until practically the whole of the fibres arising from the posterior roots and occupying the posterior columns of the cord are affected.

Centrally the degeneration of the fibres may be followed to their arborizations, but peripherally the limit of the process is uncertain. In the earliest cases of tabes dorsalis it is generally admitted that there is no degeneration of the nerve-fibres in the posterior root, but, according to Nageotte [27 and 28], at a later date the extramedullary section lying in the subarachnoid space is largely degenerated. This author holds that a "radiculitis" is constant in tabes dorsalis, and that the vitality of the central section of the nerve is thus diminished, with the result that a degeneration starts at the central arborization, and gradually extends back towards the ganglion. At the present time it may be said that such a view is untenable. The majority of writers appear to favour the view of Redlich and Obersteiner that the degeneration of the columns takes origin at the so-called "ring of Obersteiner," an apparent constriction in the posterior root at its point of insertion into the cord. A "sclerosing meningitis" is assumed to account for an injury to the root at this point. Orr and Rows [38] also favoured this place as representing the origin of the degeneration, but pointed out that at the same spot the neurilemma which clothed the nerve in the root was reflected upon the cord. They represented this absence of the neurilemma to be the cause of the site of the degeneration, since a nerve unprotected by this covering was more open to toxic influences. In view of the extensive experimental work by which this opinion is supported, it may be taken as being substantially correct, with the reservation that the point of reflection of the neurilemma does not accurately coincide with the ring of Obersteiner. The exact spot is variable in different fibres, so that one fibre of the root may be unprotected for a greater distance than another, and thus the degeneration of tabes dorsalis may extend for a variable short distance into the root.

Although statements have been made to the contrary, it is probable that there is no essential lesion of the cells in the posterior root ganglion in typical cases of tabes dorsalis. The changes observed in

later cases are merely atrophic, and secondary to the degeneration of the columns.

An early and constant feature of tabes dorsalis is the proliferation of the neuroglia of the affected columns.

The interstitial structures are also involved in the process. The pia mater over the posterior columns is always affected, and on section is found to be infiltrated with lymphocytes and plasma-cells. Perivascular collections of these cells are also commonly found about the veins, but the arterioles are usually free from obvious changes. The meninges covering the anterolateral faces of the cord are generally normal. The slight degree of meningitis which is observed over the posterior columns is also common to a variable extent in the roots, and, indeed, has been held to be the essential lesion of tabes dorsalis, both by Nageotte and by Redlich and Obersteiner.

It cannot be denied that inflammatory lesions of the roots are common, and, indeed, an actual gummatous process may occur, but they are far from constant.

The relation of the *Spirochæta pallida* to the lesions of tabes dorsalis is at present unknown. Noguchi [34] has indeed mentioned the presence of the organism in the posterior columns of one case, but, on the other hand, Versé [53] has described spirochæte-like bodies in two cases—in one in the posterior root and in the other in the ganglion. It would appear that the subject requires further investigation.

In addition to the lesions of classical dementia paralytica and tabes dorsalis, other so-called "parasyphilitic" diseases of the central nervous system are described which differ from the two main types chiefly in the area of the brain or cord involved. Thus "tabes optica" denotes a "parasyphilitic" lesion of the optic nerves. The microscopic anatomy of such lesions has been studied by Stargardt [49]. He failed to find evidence of a degeneration originating in the retina. In every case there was present an inflammatory lesion of the optic chiasma which was associated with a degeneration of the nerves at this point. The inflammation as evidenced by the type and distribution of the interstitial cells was of exactly the same nature as that observed in dementia paralytica. The degeneration of the nerves did not precede the inflammation, neither did the inflammation precede the degeneration; they were both coincident processes, due in all probability to the same cause, the *Spirochæta pallida*. Stargardt was, however, unable to demonstrate this organism.

If allowance is made for the relative obscurity of the morbid histology of tabes dorsalis as compared with that of dementia paralytica, it will be recognized from the foregoing account that the two processes are closely comparable.

In tabes is found a profound degeneration of nerve structures and an overgrowth of glial tissue. This is the outstanding lesion, but, in addition, there is a constant lymphocyte and plasma-cell infiltration of the neighbouring meninges and perivascular cell accumulations. These lesions are also the lesions of dementia paralytica, and the close similarity between the histology of the two diseases had already led many to accept the theory of a common etiology before the demonstration of the *Spirochæta pallida* in both rendered such a view almost unavoidable.

## The Comparative Pathology of the Syphilitic and "Parasyphilitic" Lesions of the Nervous System.

In the preceding section we have described three groups of diseases of the central nervous system which are due to syphilis; namely, the lesions of secondary syphilis, meningitis or encephalitis; the tertiary processes, so-called "gummatous meningitis," with which are usually associated the later secondary manifestations, and finally the "parasyphilitic" conditions, dementia paralytica, tabes dorsalis and other varieties. The question now arises, what is the relation between these three groups?

### *Secondary Syphilis of the Nervous System.*

Although it must be admitted that the precise pathology of the early syphilitic lesions of the brain and spinal cord already referred to is a field of neurology which requires much elucidation, nevertheless it is clear that they may be divided into two main groups, an acute condition which rapidly leads to stupor and death, and a subacute lesion which may only be indicated by irritability and headache. In the latter there is no indication of an affection of nerve-cells; it is probably due entirely to a slight meningitis, that is to say to a slight meningeal or interstitial infiltration due to the presence of spirochætes about the vessels in the membranes. On the other hand, in a more acute lesion, the spirochætes may wander from the lymphatics surrounding the vessels in large numbers and may invade the actual neurons of the brain. In this way true encephalitis may arise and according to its severity or distribution may give rise even to fatal symptoms.

In the secondary period, therefore, the brain may be looked upon as being prone to a subacute lesion which mostly affects the interstitial tissues and also an acute lesion of greater extent which involves not only the interstitial but also the parenchymatous structures. In this manner it may be said that the early lesions of the brain are very similar to those of the liver; on the one hand is the acute parenchymatous lesion leading to acute atrophy and death, and on the other the interstitial inflammation which may only be detected by the occurrence of a slight jaundice.

The later secondary affections of the brain and cord may be looked upon entirely as interstitial lesions. They are associated with more infiltration and proliferation than the early lesions and thus lead to secondary interruption of nerve structures, and consequently to well-marked localizing signs—cranial palsies, root lesions, &c.

*Tertiary Lesions of the Central Nervous System.*

The relation of these affections to the tertiary affections of other organs is close. They consist of foci, relatively discrete or fused, which develop about a blood-vessel as a result of an exacerbation of spirochætes in or about its walls. The process is essentially focal, although the conglomeration of foci may lead to a diffuse result; but, however diffuse, there is very little tendency for the lesion to progress beyond the confines of the interstitial tissues in which it takes origin. The common name "gummatous meningitis" is, however, incorrect, in that the inflammation may extend from the meninges along the perforating vessels into the brain or cord, and, indeed, in rare cases these vessels may be involved alone while the meninges escape.

It is probable that when evidence of nerve degeneration is detected, this is a secondary process due merely to pressure of exudates or interruption of blood-supply. In the case of the liver there is indeed a primary destruction of such parenchymatous cells as find themselves within the zone of toxic influence, but in the nervous system, as will be noticed later, there is a sharper anatomical separation between parenchymatous and interstitial tissues, and therefore the gummatous process tends to be more purely interstitial than in other organs.

If, however, allowance is made for slight differences due to variety in anatomical structure, it is clear that the gummatous lesions of the central nervous system are strictly analogous to those chronic focal processes in the various internal organs in which the incidence of the

intoxication falls almost entirely upon the interstitial tissues, e.g., the more or less focal "gumma" of the liver. The expression "gummatous meningitis" may, therefore, be correctly superseded by the term "chronic syphilitic interstitial encephalitis or myelitis."

### "*Parasyphilis.*"

While the gross and microscopic appearances of brains and spinal cords affected with "parasyphilis" are on the whole well known, the exact nature of the process is very much *sub judice*. The literature dealing with this subject is enormous, and it will be possible to deal only with the question in its broader aspects. The reader who requires a detailed survey of the relation of "parasyphilis" to syphilis may be referred to the Report of Nonne to the Section of Neuropathology of the recent International Congress of Medicine [37].

It would appear that one group of pathologists, especially perhaps those of the French school, look upon dementia paralytica as an encephalitis, or *inflammation* of the brain, while others, German and English, hold the view that the whole process is *degenerative*.

With regard to the "*inflammatory*" theory opinion is divided as to the primary lesion, that is to say many hold that the nervous tissues proper are the seat of the initial lesion, while the increase and activity of the interstitial tissues and neuroglia is secondary. This group favours the term parenchymatous encephalitis. Others, on the other hand, hold that the initial process is interstitial, perhaps vascular or lymphatic, and this leads to a secondary degeneration of the nerve elements.

Those who hold the "*degenerative*" view assume a pathological process which must be looked upon as abnormal. They consider that the degeneration of the nervous tissue is *primary* and is not the result of an antecedent inflammation. Although it is difficult to find examples of primary degeneration in other fields of pathology, it is assumed that the nerve-cell, being a highly specialized structure, is abnormal and can undergo this process simply as a result of unfavourable environment of long standing. According to this view the proliferation of neuroglia is secondary, and the meningeal and perivascular changes are of the same nature.

The precise effect of syphilis in the causation of the brain lesions appears to lead to as much dispute as does the interpretation of the lesion itself.

On all sides it is admitted that syphilis is an essential in the etiology of the disease, but as to whether the *Spirochæta pallida* is the immediate

irritant, or whether the process results from a hitherto unrecognized ultimate effect of this organism is not definitely known.

Those who hold the "inflammatory" view, whether interstitial or parenchymatous, presume a direct activity of the spirochæte exercised in an abnormal form, while the "degenerative" theory presumes that a weakness of the cells results from a "constitutional syphilis" or prolonged action of "toxin," and that the actual degeneration is occasioned by accessory factors of stress (alcohol, trauma, "exhaustion," &c.). In general the type of lesion is considered not to be "syphilitic."

Recently the concept of "parasyphilis" as an active syphilitic lesion has been supported by Stargardt [49]. This author found the "parasyphilitic" lesions of the optic nerve to be due to a chronic inflammation of the same type as that found in the brain in dementia paralytica, an inflammation due to the virus of syphilis. Again, Schoenborn and Cuntz [47] disputed the existence of a "parasyphilis" in the sense of Fournier; they pointed out that the concept rested almost entirely upon the incurability of the condition and the difficulty in demonstrating the virus. Cuntz [4] argued that most of the "parasyphilitic" diseases of Fournier in the internal organs are now known to be actively syphilitic, and therefore that the nervous lesions were probably of the same nature.

From our analysis of the essential cell reactions of syphilis in Chapter I, it will be seen that one of the chief characteristics of these reactions is the perivascular distribution. A small vessel is found with a proliferated endothelium, the local fixed connective tissue cells are also proliferated while the surrounding lymphatics are laden with plasma-cells and lymphocytes. This is the reaction of the interstitial cells. Turning now to the account of the histology of "parasyphilis" it will be seen that the interstitial reaction in the meninges and about the vessels is closely analogous. Thus in our view the interstitial lesion of parasyphilis may be described correctly as "syphilitic." Again, on consideration of the nerve lesion and neuroglial proliferation in these cases we find striking resemblances to those tertiary syphilitic lesions of internal organs in which, owing to a diffuse distribution of the virus, the parenchymatous lesion is more striking than the interstitial, and we have evolved the view that the lesion of parasyphilis is a tertiary syphilitic parenchymatous inflammation, not of an abnormal or "nongummatous" type, but of essentially the same nature as parenchymatous lesions of all organs due to tertiary syphilis [22 and 23].

*Dementia paralytica.*—As we have already pointed out in the case

of the liver and other organs the *Spirochæta pallida* produces parenchymatous and interstitial reactions in all cases, but in some the effect may be most marked upon the parenchyma, while in others upon the interstitial tissues. These different effects are due to the distribution of the spirochætes. In those organs in which parenchyma and interstitial tissues are closely related, the two types of reaction will be somewhat confused and will commonly occur together in the same process.

In the case of the brain, however, we would point out that the parenchymatous nerve tissues, together with the neuroglia, are developmentally and anatomically separated from the interstitial tissues proper, that is, the vascular-lymphatic structures. In the process of development the vessels grow from the meninges into the cortex and push before themselves the innermost layer of the pia and the limiting neuroglial membrane of Lenhossek. These tissue layers are represented by the wall of the perivascular adventitial sheath and the insertions of the neuroglia upon it, and these structures form a barrier more or less impenetrable between the lymphatics in the adventitial sheath and the ganglion cells and neuroglia.

Thus in the brain there is an abnormal separation of parenchyma and interstitial tissues, and this will lead to an unusually distinct effect of the *Spirochæta pallida* upon the two tissues according as it finds itself on one side or other of the anatomical barrier; if in the nervous tissues the chief lesion will be parenchymatous, if in the lymph-vascular tissues the lesion will be chiefly interstitial.

Now from the recent researches of Noguchi and others it is established that the spirochætes in dementia paralytica tend to be limited to the nervous tissues and are rarely found in the lymphatics or meninges, thus it is clear that the chief effect of the organism will be expended upon the ganglion cells and neuroglia in the brain substance proper.

According to our view an exacerbation of the virus in the brain leads to an immediate reaction in the sense of inflammation of the nerve-cells and neuroglia. The swelling of the ganglion-cells may mark this reaction and may be equivalent to the "cloudy swelling" of other inflamed parenchymatous cells. The reaction will, however, be abortive; the intoxication will be greater than the cells can sustain and a *secondary* degeneration will soon set in. The neuroglia may be looked upon as a special type of interstitial tissue and the reaction in this case will lead to a proliferation. This process is equivalent to a reaction of fixed interstitial cells. Since now a toxic focus is in

a state of activity the wandering cells will be attracted to the area from the surrounding lymphatics. These cells, lymphocytes and plasma-cells, will be found in the lymphatics of the meninges and perforating vessels streaming towards the focus. They cannot, however, attain it in the brain as they can in other organs, owing to the more or less impenetrable barrier already referred to; thus the process will tend to remain diffuse and no localized collection of cells or gumma will be produced, neither will the distribution of the spirochætes correspond to that of the cell infiltrations, as we have already observed. No doubt, a certain degree of proliferation of the fixed cells in the lymphatics will occur in some cases owing to diffusion of the toxin or a wider distribution of the spirochætes, but the general active effect in the lymph-vascular tissues will not be marked, the process there will be more or less passive. The amount of active reaction of the interstitial cells will depend upon the chronicity of the disease. In the most rapid cases it will be least pronounced.

According to the view enunciated the lesion of dementia paralytica is as typically syphilitic as a lesion of the liver. It occurs as an inflammatory reaction about the *Spirochæta pallida* situated among the nerve-cells, but its effect is most marked upon the parenchyma because this tissue is abnormally distinct from the interstitial tissue. A reaction of the parenchyma rapidly leads to degeneration as in the liver, while the reaction in the fixed neuroglial tissues produces proliferation. The wandering cells fill the lymphatics as in other organs, but cannot reach the toxic focus and so produce a "gumma."

We therefore refer to dementia paralytica as a tertiary syphilitic parenchymatous encephalitis, and had already arrived at this conclusion before the demonstration by Noguchi of the *Spirochæta pallida* in the brain. We were of the opinion that, in view of the technical difficulties experienced in applying Levaditi's staining method to the brain, the mere fact that the virus could not be demonstrated was a matter of little importance.

*Tabes dorsalis.*—In dementia paralytica we have described the lesion as an inflammatory reaction of the nerve-cells and neuroglia, and, to a slight extent, of the lymph-vascular tissues to the stimulus of the *Spirochæta pallida* situated among the nerve-cells. In our view the essential lesion of tabes dorsalis also is due to an inflammatory reaction on the part of the nerve-fibres and neuroglia induced by the presence of the *Spirochæta pallida*. As in the case of the brain, the neuroglia will proliferate, but the intoxication of the nerve-fibre will lead to its

destruction. Some degree of reaction may be observed in the fixed lymph-vascular tissues, and the lymphatics of the meninges will be infiltrated by wandering cells as already described in dementia paralytica.

The degeneration of the nerve-fibres following on this intoxication will occur in those parts only which have been deprived of the neurilemma. It is known that the neurilemma is a structure of primary importance in the regeneration of nerves, and it is probable that it also exerts a protective and nutritive function, and thus if a sublethal intoxication of a neuron occurs the part which is unprotected by the neurilemma will suffer, rather than the protected portion. In this manner it is easy to account for the fact that the degeneration ceases where the neurilemma clothes the nerve, as pointed out by Orr and Rows [38].

These authors were able to show that in early cases of dementia paralytica changes were always present in the cord which were identical with those found in the earliest lesions of tabes dorsalis. These changes consisted of parenchymatous degenerations of the posterior columns, and in every instance the degenerative lesion originated at the point of loss of the neurilemma. From other papers by the same investigators it is clear that exactly similar cord lesions or lesions of the comparable cranial nerves may follow spontaneously as a result of an intoxication of the spinal cord or brain by the products of septic foci situated in the skin [39], and indeed such lesions may be produced by introducing bacterial toxins into the perineural lymph channels of the afferent nerves [40]. In all such cases in which a "tabetic" lesion is produced by a peripheral septic focus, the toxins ascend to the posterior columns of the cord by the lymphatics of the peripheral nerves without these nerves being themselves obviously injured. The existence of this afferent perineural lymphatic system had been previously noted by Homén and Laitinen [14] and was confirmed by Orr and Rows. On these grounds Orr and Rows [41] have looked upon dementia paralytica and tabes dorsalis as chronic inflammatory lesions due to a toxic substance ascending the lymph-stream; in any case it is clear from their work that the morbid agent which induces the degeneration is distributed by the lymphatic rather than by the blood-stream, and indeed the same conclusion had already been stated in much less detail by Marie and Guillain [25]. Tabes dorsalis was a lesion of the lymph system which comprised the posterior columns, the membranes covering them and the posterior roots.

Since therefore the parenchymatous degeneration and also the adventitial changes of tabes dorsalis and dementia paralytica, namely the proliferation of the glia and the plasma-cell and perivascular proliferation, may all be produced experimentally by the introduction of bacterial toxins into the afferent lymphatics, it is clear that the *Spirochæta pallida*, operating in the same anatomical areas, may be assumed to be the actual cause of the two diseases under discussion, especially when it can be shown that the lesion produced is strictly comparable to the lesions produced by the same virus in other internal organs.

## Classification of the Syphilitic Diseases of the Central Nervous System.

According to the views expressed in the previous pages "parasyphilis" has no separate existence from the other syphilitic diseases of the central nervous system so far as its pathology is concerned. It is a tertiary process resulting from a more or less diffuse distribution of spirochætes within the nervous tissues as opposed to the gummatous lesions which result from an inflammation located in the interstitial tissues. These two are similar lesions occurring in different tissues and thus leading to very different results. If the "gummatous meningitis" of the brain may be referred to as "chronic interstitial encephalitis" so may "parasyphilis" be described as "chronic parenchymatous encephalitis or myelitis."

Although the processes are often distinct, nevertheless there is reason to believe that they are quite commonly combined. "Meningitis," for instance, is frequent in tabes dorsalis. In such cases it may be assumed that the distribution of the spirochætes is more general than usual; they may be present both in the meninges and also in the brain substance, and thus may produce both types of "tertiary" lesion at the same time.

We have already stated [8] that an associated parenchymatous and interstitial lesion may be assumed when, as a result of treatment in "parasyphilis," the Wassermann reaction in the cerebrospinal fluid is rapidly reduced in intensity up to a certain point beyond which it is persistent. Such cases are relatively common, and we have recently been able to observe *post mortem* the accuracy of this assumption. On reference to Case 90[1] it will be seen that the reaction behaved in this

[1] A reference to this case will be found in *Brain*, 1914, vol. xxxvii, p. 124.

manner, and at the autopsy a typical dementia paralytica was disclosed but associated with a marked interstitial lesion.

The relationship between the lesions produced by syphilis may, therefore, be tabulated as follows:—

*Lesions of the Secondary Period.*

(1) Interstitial encephalitis or myelitis ("meningitis").

(2) Parenchymatous encephalitis or myelitis ("encephalitis," "myelitis").

*Lesions of the Tertiary Period.*

(1) Chronic interstitial encephalitis or myelitis ("gummatous meningitis").

(2) Chronic parenchymatous encephalitis ("dementia paralytica").

(3) Chronic parenchymatous myelitis ("tabes dorsalis").

### Conclusions.

We have shown that the central nervous system is affected by syphilis at the same periods and in the same manner as are other internal organs. In addition the "parasyphilitic" lesions are also of a typically syphilitic nature, being directly comparable to the parenchymatous affections found elsewhere in the body. They are "tertiary" lesions differing only from the so-called "gummatous" processes in the central nervous system in that their localization is in the parenchyma while that of the latter is in the interstitial tissues.

## Chapter IV.—Allergie in the Syphilitic Diseases of the Nervous System.

In describing the syphilitic lesions of the internal organs we have shown that the amount and to some extent the quality of the reaction to the *Spirochæta pallida* is variable in the different stages of the disease. In the acute stages when the number of spirochætes is maximal, the tissue reaction is relatively slight, while in the chronic conditions a very marked and destructive lesion occurs although the number of causative spirochætes is small. This result is due to an alteration in the susceptibility of the tissues, called by von Pirquet "allergie."

The same disproportion between cause and effect is noticeable in the syphilitic lesions of the brain and spinal cord.

In the encephalitis of the secondary period the amount of cell reaction is slight, and yet there is reason to suppose that the spirochætes

present in the brain are as numerous as in other secondary conditions. In the tertiary interstitial encephalitis, on the other hand, the spirochætes are relatively few, although the reaction of the tissues is great. Again in the chronic parenchymatous lesions, dementia paralytica and tabes dorsalis, the extent of the lesion is great and yet the number of spirochætes is usually, as is well known, extremely small. There is thus the same lack of relation between the extent of the lesion and the amount of the virus as is observed elsewhere in syphilitic lesions. Those of the central nervous system are also under the influence of allergie.

As already described in previous chapters, the state of hypersusceptibility of the tissues generally, follows as an immunity response to the destruction of spirochætes at the time of the exanthem. In order to apply this argument to account for the chronic interstitial and parenchymatous nerve lesions, however, it will be necessary to bring evidence of a previous syphilitic inflammation of these regions during the acute stage, since the tertiary exacerbations are due to spirochætes which have remained dormant *in situ*, affecting tissues which have been previously sensitized. Such a previous involvement has already been described as a slight encephalo-myelitis occurring in the secondary stage. The lesion may be of such an intensity as to lead to appreciable symptoms; on the other hand, it may be so slight as to escape direct notice and is then merely a factor in the production of the syphilitic cachexia. Since the virus is blood-borne and part of the general dissemination during the acute stage, the interstitial tissues of the brain are mostly affected, and therefore the interstitial tissues will most often bear the brunt of the subsequent exacerbation as found in "gummatous meningitis."

It may, however, be readily understood that in certain patients a few of the spirochætes may wander from the adventitial lymph sheaths of the vessels and actually penetrate the confines of the ganglion-cells and neuroglia. The primary nervous affection in such a case may be too slight to produce noteworthy manifestations, but it may, nevertheless, be sufficient to determine the site of the exacerbation in the parenchyma at a later date and the production of dementia paralytica.

One of the chief objections which have been advanced against the inflammatory view of "parasyphilis" is the curious localizations of many of the lesions in "systems" of nerves, but a possible explanation may be found in the work of Orr and Rows. It will be remembered that these authors have demonstrated the existence of a direct lymphatic path from the skin to the central nervous system along the afferent

nerves, and by introducing bacterial toxins into this lymphatic system they have produced central lesions which are directly comparable to those of dementia paralytica and tabes dorsalis. Further, in certain chronic skin lesions (bed sores) they have observed the spontaneous development of such central lesions, and have put forward the view that the parasyphilitic diseases are due to a chronic inflammation of lymphogenous origin. The bearing of these results upon the localization of certain manifestations of "parasyphilis" is important.

The skin in secondary syphilis is, even in the absence of a rash, the site of innumerable spirochætes, and judging from the accounts of Ehrmann [5] and Levaditi [20], in which they described the *Spirochæta pallida* lying in the nerve-sheaths of the primary sore, it may be assumed that these spirochætes readily find their way into the sheaths of the nerves in secondary syphilis also. In this manner they gain a direct path to the central nervous system, as was, indeed, pointed out by Ehrmann, and since the lymphatics follow the course of the nerves it is easy to understand that the distribution of the subsequent "parasyphilitic" exacerbation will follow that of systems of nerves.

Although we consider that the blood-borne secondary encephalitis is the more probable explanation of the distribution of the lesion in dementia paralytica, it is clear that some of the more localized "parasyphilitic" lesions (primary optic atrophy, &c.) are more readily explained on the lymph-borne theory of Orr and Rows. Spirochætes derived from the skin of the face, the buccal cavity or tonsils may easily reach central areas by way of the cranial nerves and there lie dormant. An exacerbation at a later date will then develop into a local tertiary gummatous lesion if the virus is confined to the lymphatics, or a tertiary parenchymatous lesion if a few spirochætes have wandered from the lymphatics into the nervous substance proper.

The peculiar distribution of the tabetic lesion has always given rise to much discussion; but since the skin in the secondary period and also many of the internal organs harbour the spirochæte, it is easy to assume that these organisms may reach the posterior columns of the cord by the afferent perineural lymphatics and induce a slight myelitis in this position which usually escapes notice. Further, as in the brain, a few of the spirochætes may wander from the adventitial lymphatics and actually affect the nerve-fibres themselves. If such a distribution occurs a later exacerbation of these spirochætes will produce the large reactive lesion and subsequent degeneration which occasion the symptoms of tabes dorsalis. There is, in fact, very direct evidence that

such a lymphatic inflammation is common in the secondary period without producing symptoms. As is well known, syphilis in the rabbit is apparently a local disease which proceeds to spontaneous cure, and yet Steiner [50] has examined a number of these animals and found inflammatory lesions of the perineural lymphatics of the roots, which spread into the cord as adventitial collections of cells. Analogous lesions were found in the brain. The distribution of those lesions in the lymphatics is highly suggestive that the virus ascended the afferent nerves, as described by Orr and Rows in the case of bacterial toxins.

It will be understood that we have introduced the concept of a sensitization of the nerve tissues merely in order to account for the remarkable extent of the lesion which follows at a later date as a result of an exacerbation of a relatively small number of spirochætes, but nevertheless a lesion of a similar type might conceivably follow from a chronic absorption of toxin from the lymph system in the sense of Orr and Rows.

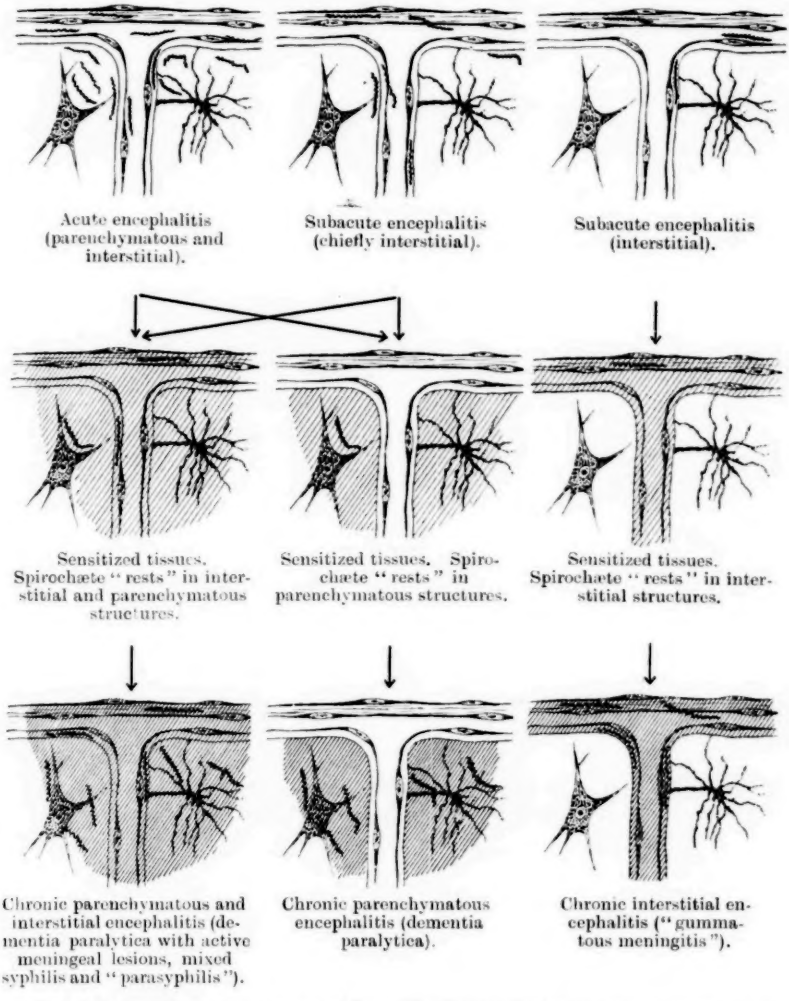
The lesions of the spinal cord produced experimentally by Orr and Rows resulted from the absorption of diffusible toxin derived from pathogenic bacteria and not from the activity of the bacteria themselves. In the case of syphilis, however, it is doubtful whether a "toxin" exists of such potency that it can effect a profound lesion at a distance. If, however, in the theory of Orr and Rows we insert the word "virus," instead of "toxin," it would follow that tabes dorsalis and dementia paralytica might be the result of a very chronic syphilitic inflammation of the special lymphatic system. The objection to such a view is that there is no source for this virus except in the secondary period, and it would seem improbable that a chronic action would continue during the whole interval of time between the secondary period and the onset of tabes dorsalis or dementia paralytica without producing symptoms.

The lesion of early tabes dorsalis and dementia paralytica appears to be too acute to be explained by an extremely slow irritation lasting many years. It suggests an exacerbation, and since the number of spirochætes causing this exacerbation must be small, we endow the issues with the state of hypersusceptibility and have adduced considerable evidence that such a state is general in chronic syphilis.

## Conclusions.

The "parasyphilitic" diseases are due to an exacerbation of *Spirochæta pallida* about nerve elements which are in a state of hypersusceptibility. This state is induced as a reaction to an intoxication

DIAGRAMS OF THE EFFECT OF ALLERGIE UPON SYPHILITIC LESIONS OF THE CENTRAL NERVOUS SYSTEM (BRAIN).



Acute encephalitis (parenchymatous and interstitial).

Subacute encephalitis (chiefly interstitial).

Subacute encephalitis (interstitial).

Sensitized tissues. Spirochæte "rests" in interstitial and parenchymatous structures.

Sensitized tissues. Spirochæte "rests" in parenchymatous structures.

Sensitized tissues. Spirochæte "rests" in interstitial structures.

Chronic parenchymatous and interstitial encephalitis (dementia paralytica with active meningeal lesions, mixed syphilis and "parasyphilis").

Chronic parenchymatous encephalitis (dementia paralytica).

Chronic interstitial encephalitis ("gummatous meningitis").

Each diagram represents schematically a section of the cerebral cortex. A nerve-cell on the left hand is separated from a neuroglia cell on the right hand by a vascular prolongation of the meninges which form the upper boundary of the figure. Spirochætes are represented by wavy lines.

The top row of figures represents the conditions in the early period of syphilis in which a variable number of spirochætes act upon non-sensitized tissues.

In the second row of figures the shaded parts represent the various sensitized tissues in which "rests" of spirochætes are lodged (latent period of syphilis).

In the third row of figures these sensitized areas are now thrown into reaction by the renewed activity of the spirochætes.

occurring in the secondary period, and the spirochætes taking part in the exacerbation are remnants of those which produced the original intoxication.

The path of invasion of the central nervous system may be twofold. Firstly, the spirochætes may reach the nerve elements by the blood-stream as part of the general dissemination of the secondary period, or secondly, they may reach these structures during the same period by direct spread up the perineural lymphatics. The interstitial nervous lesions of tertiary syphilis are due to a similar process affecting these tissues only.

## Chapter V.—The Effect of Treatment upon Syphilitic Diseases of the Nervous System.

In previous sections we have endeavoured to show that fundamentally the lesion of "parasyphilis" is an inflammatory process in every way comparable to the other lesions of syphilis, and it will therefore be necessary to inquire into the conditions which permit of successful treatment in the one case, but not in the other.

It will be remembered that the incurability of the "parasyphilitic" lesion constituted one of the main distinctions from syphilis according to the original view of Fournier, and this standpoint has been accepted by most authorities up to the present day, to such an extent that, before the introduction of salvarsan, to apply antisyphilitic treatment to a patient diagnosed as suffering from a "parasyphilitic" condition was the exception.

When the concept of "parasyphilis" as introduced by Fournier is examined, it must be generally admitted that the definition is peculiarly crude. Thus he classes under this heading not only tabes dorsalis and dementia paralytica, but also pigmentary syphilides and a large number of syphilitic and non-syphilitic states which are now entirely forgotten in this connexion. The only discoverable similarity between the parasyphilitic conditions of Fournier is a common, but not essential, derivation from syphilis and a general insusceptibility to antisyphilitic treatment. At a later date (1903) very much the same attitude was adopted by Hermanides, but in his classification a further series of pathological states were included, such as chronic superficial glossitis and amyloid degeneration of the internal organs.

The concept of "parasyphilis" as propounded by Fournier and Hermanides has lately been investigated by Cuntz [4]. This author

shows in detail that the application of the term "parasyphilis" to certain diseases of internal organs is fallacious, since these diseases are purely syphilitic and directly due to the *Spirochæta pallida*.

We therefore discard the original definition of "parasyphilis" and discuss it in its modern aspect as relating to diseases of the nervous system only.

As already mentioned, the most pronounced distinction between "parasyphilis" and syphilis is the futility of antisyphilitic treatment in the former case. The disease is looked upon as being progressive in spite of the most drastic treatment, even applied in the earlier stages, and in fact it has become the common practice to omit such treatment as being useless and sometimes leading to undesirable results.

When the nature of the "parasyphilitic" lesion is considered, the reason for this futility is clear. The symptoms of dementia paralytica and of tabes dorsalis are due to degeneration of nerve elements situated in the central nervous system, and since such structures have no power of regeneration, no remedial measures can prevent the progress of the degeneration to the furthest limits of the neuron.

Such an effect is not, however, in any way characteristic of "parasyphilis" alone, since the same result follows any other lesion of the central nervous system and all such are equally refractory to treatment. Neither is the progressive degeneration of the neurons characteristic only of the central nervous system. The nervous tissue is merely the highly specialized parenchyma of the brain and is comparable to the highly specialized parenchyma of other organs. It may be taken as a general rule that the more a cell is specialized for a particular function, the less developed is its power of resistance to injury or of regeneration. The parenchyma of the liver and kidney, for instance, display a similar "delicacy" to that of the brain. The cells of these organs, when injured beyond a certain point, degenerate and eventually may be entirely replaced by fibrous tissue; no amount of mercury will "cure" a chronically inflamed kidney in the sense that it will produce a *restitutio ad integrum* of the secreting tubules. The kidney and liver, however, differ from the central nervous system in that they contain a large number of cells performing the same function, and therefore a destruction of many of these will produce no obvious effect. Their work will be undertaken by the remaining cells. Further, these organs may not only respond by an increased functional activity per cell, but an actual new formation of cells may occur. In the central nervous system, however, not only is no new formation of cells observed, but

function is so specialized that a destruction of any group of cells will immediately lead to outward manifestations of the lesion. Perhaps the nearest parallel to the nervous system is found in the testicle. A diffuse parenchymatous lesion of this organ is immediately recognized by sterility. The degeneration of the cells is progressive and is not affected by antisyphilitic treatment, so that a lesion of a certain intensity will lead to a complete loss of the spermatogenic function.

The incurability of the symptoms of dementia paralytica or tabes dorsalis does not therefore call for any further remark than does the sterility following syphilitic orchitis. If the one is to be termed "parasyphilitic" the name will equally apply to the other; but no useful purpose will follow such application, and if the term is held to imply any pathological state other than a secondary parenchymatous degeneration following injury, we hold that it should be discarded. Again we look upon the expression "progressive" as applied to "parasyphilitic" diseases as not strictly accurate. The intention is to show that dementia paralytica or tabes dorsalis once started will proceed to death. Strictly, however, the term is only applicable to the condition of each affected neuron. The degeneration of each neuron once started will be progressive until the whole unit is destroyed, but the process will not necessarily spread to contiguous neurons. To illustrate this fact it is only necessary to call attention to certain cases of primary optic atrophy and other "parasyphilitic" diseases of isolated nerve groups which do not progress. The apparent progress of the lesion in dementia paralytica and tabes dorsalis is clearly due, not to a spread of the degenerative process from neuron to neuron, but to a continued activity of the primary intoxication which leads to the secondary degeneration, in fact to *a continuation of the syphilitic inflammation in spite of treatment.*

Before discussing this aspect of the problem in more detail it will be necessary to inquire to what extent the futility of antisyphilitic treatment is completely established.

Before the era inaugurated by the epoch-making discoveries of Ehrlich and Wassermann, the treatment of "parasyphilis" was almost entirely symptomatic or palliative for the reason that the essential relation between syphilis and parasyphilis was not always accepted and because the relatively feeble antisyphilitic remedies of that time were ineffective. Since the introduction of the Wassermann reaction, however, few are found who dispute the dependence of "parasyphilis" upon syphilis, and in addition a large number of authors have described

a definite beneficial effect of salvarsan. In our view some at least of these successful therapeutic results must be ascribed to a confusion of diagnosis between "parasyphilitic" and "true syphilitic" diseases of the nervous system. It cannot be denied that in certain cases the differential diagnosis is extremely difficult and any marked and lasting improvement in a supposed case of "parasyphilis" should at once call for further investigation into the symptoms upon which the diagnosis has been based. On the other hand marked improvement in the condition of a "parasyphilitic" may be due to the resolution of an interstitial nervous syphilis associated with the parenchymatous condition. In the series of Dr. Head and Dr. Fearnsides several such cases of mixed "parasyphilis" and syphilis will be observed in which as a result of treatment, or even without, the condition of the patient much improved. This recovery is accompanied by a quantitative diminution in the strength of the Wassermann reaction in the cerebrospinal fluid and a decline in the cell count, but the clinical and pathological improvement is apt to proceed only to a certain point, when the condidition again becomes stationary. One such patient (case 90) died of dementia paralytica, and at the autopsy the marked interstitial lesions were demonstrated. We have, therefore, formed the opinion that when a case of "parasyphilis" shows definite pathological improvement after treatment, this result is due, not to any great alleviation in the "parasyphilitic" lesion, but to a resolution of an associated interstitial syphilis.

In general we consider that antisyphilitic treatment of pure dementia paralytica, for instance, is futile, but this result is very largely due to the fact that the nerve degeneration is of such a distribution that vital functions are early involved. The lesion even in its earliest stage is hardly compatible with continued life. In the case of tabes dorsalis, however, the outlook is different. In an early stage the nerve lesion is not necessarily fatal, and if it were possible to arrest the syphilitic process, which accounts for the progress of the lesion, it would be possible to cure tabes dorsalis; that is to say, to leave the condition *in statu quo*.

In view of the chronicity of this state it is impossible to judge to what extent this result is possible at the present day, but many must have succeeded by repeated salvarsan injections during the past two or three years in maintaining early cases of tabes dorsalis in a stationary condition.

Although, therefore, it will be generally admitted that "parasyphilitic"

states are undoubtedly refractory to treatment, it does not follow that such treatment is entirely without effect. In the paper dealing with a study of the Wassermann reaction in such conditions [7] it will be seen that we have been unable to show any definite result of treatment, as evidenced by a diminution of the strength of the Wassermann reaction in the cerebrospinal fluid, nevertheless it will be observed that after lapses of time longer than we have been able to record in any fresh case, the reaction may be found to be negative, and this finding will coincide with a stationary condition of the manifestations. If the activity of the disease may subside naturally, it is not unreasonable to suppose that this subsidence may be assisted by treatment.

If, then, it is allowed that therapeutic measures may have some beneficial effect, it is still anomalous that this effect should be so small compared with the rapid improvement in cases of cerebrospinal syphilis, in particular when we have described the two processes as being fundamentally the same.

We have already shown that a tertiary interstitial lesion of the brain is curable while a tertiary parenchymatous lesion is not; that is to say, in the former the Wassermann reaction in the cerebrospinal fluid rapidly becomes negative, while in the latter it is uninfluenced [7].

This characteristic of "parasyphilis" is constant, and indeed may be said to be diagnostic, so far as the central nervous system is concerned; nevertheless it does not distinguish "parasyphilis" from tertiary interstitial syphilis in other parts of the body, because in certain types of the latter condition treatment is equally ineffective. It is notorious that when the reaction in the serum of a tertiary syphilitic is estimated quantitatively during the course of treatment, the decline in its intensity is usually very slow, or may be entirely absent. In such cases equally with "parasyphilis" it may be argued that treatment is ineffective. This result is the more surprising when it is remembered that the visible lesions, gummata of the skin, rapidly heal after a single dose of salvarsan, and yet the reaction may remain persistent. In our opinion the explanation of this phenomenon depends upon the existence of tertiary syphilitic processes within the body in areas which are anatomically secluded from the effect of an antisyphilitic substance in the blood-stream; thus, although widespread lesions of the skin may be at once resolved, the reaction is still maintained in almost undiminished intensity by hidden foci in other parts of the body.

Such a focus may commonly exist in the aorta. Clinically it is well known that the reaction is most resistant in cases of aneurism and

aortitis, and, moreover, with Turnbull (unpublished) we have found that aortitis is by far the commonest syphilitic lesion in the *post-mortem* room. From this result we conclude that a tertiary syphilitic may commonly suffer from a resistant lesion of the aorta, which will maintain his Wassermann reaction in full intensity in spite of the resolution of other foci. Such a patient would compare with another in whom the Wassermann reaction was maintained by a parenchymatous nerve lesion in spite of the resolution of the interstitial lesion.

On general grounds it might be argued that if one particular area of the body is selected by the *Spirochæta pallida* as a suitable nidus for its vegetation, that area is most likely to be secluded from noxious influences circulating in the blood-stream. In fact, we thought it probable that salvarsan or mercury did not penetrate into the wall of the aorta in sufficient quantity to destroy the spirochætes, and thus that the incurability of aortitis was due to the lack of penetration of the drug. We therefore submitted the organs of certain patients who had died after salvarsan injections to Dr. W. H. Willcox for analysis, and he has found that the aorta contained no arsenic, although other organs were heavily charged therewith (unpublished observations). Such a result supports our view that the persistence of the lesion in the aorta is due to the inability of drugs (and perhaps natural agencies) to reach the spirochætes in the focus.

It will be remembered that in 1911 [21] we were able to announce that, according to the analyses of Dr. Willcox, the brain contained no arsenic after intravenous injections of salvarsan. From this circumstance, which we have since repeatedly confirmed on man and animals, we argued that salvarsan was not fixed by the brain, and was therefore not a neurotropic substance. From continued (unpublished) investigations, however, it is clear that this deduction is incorrect. We have found that if salvarsan is mixed *in vitro* with brain substance, a strong fixation will occur, and thus the absence of arsenic from the brain during life must be due to an inability on the part of this drug to penetrate into the brain. Indeed, if the arsenic does obtain access to the brain, as happens when the drug is inserted into the cerebrospinal fluid, immediate symptoms of toxicity are apparent. As is well known, no arsenic is normally found in the cerebrospinal fluid after intravenous injections of salvarsan; and it is often stated that this is the explanation of the absence of arsenic from the brain. It is supposed that the cerebrospinal fluid functions as a lymph of the brain, and that

substances which enter this organ must do so by way of the choroid plexus and the cerebrospinal fluid. In our opinion, however, this explanation is incorrect. In the course of our investigations we have frequently introduced drugs into the brain substance by the intravenous route, and have never found these drugs to be present in the cerebrospinal fluid. On the other hand, we have met with substances which, like arsenic, will not enter the brain or cerebrospinal fluid, although other organs of the body have contained large quantities. We have, therefore, been led to the conclusion that salvarsan after intravenous injection will not enter the brain substance because of some peculiarity of the cerebral vessels in relation to the drug. The fact that salvarsan is not found in the cerebrospinal fluid has no bearing upon the question.

The effect of these experiments upon the treatment of parenchymatous lesions of the central nervous system is clear. The progress of the lesion cannot be influenced, because drugs cannot penetrate and destroy the spirochætes which are causing this progress. Thus the incurability of "parasyphilis" and of aortitis depends upon the same factor. Similarly the frequent incidence of these two conditions is due to the same cause. When spirochætes succeed in invading the nervous system or aorta in the early stages of syphilis, they have every opportunity for vegetating in these situations until they are thrown into activity at a later date.

Very recently the injection of "salvarsanized serum" into the cerebrospinal fluid has been advocated in the treatment of parenchymatous lesions of the brain. The patient receives an intravenous injection of salvarsan. He is bled one hour later and his serum, diluted and heated, constitutes the therapeutic agent.

The rationale of the method does not appear to be satisfactorily explained. The cerebrospinal fluid is selected as the vehicle because of the prevailing assumption that this is the normal route of entry into the brain, while the "salvarsanized serum" is preferred to the crude drug because it is said to be less toxic and endowed with special therapeutic properties.

We have assisted at the treatment of patients by this method and have failed to observe any obvious justification for it. We have been unable to differentiate the improvement which often follows the initial intravenous dose from the superimposed improvement which is said to arise out of the intrathecal injection.

That the serum has a certain therapeutic effect is probable, since it contains small quantities of salvarsan, but whether these small

quantities of arsenic in the serum have any advantage over an equivalent quantity of crude neosalvarsan is certainly not proved. As shown by Wechselmann, traces of neosalvarsan may be injected intrathecally without harmful results, but when the quantity is increased for the purpose of attaining a more satisfactory therapeutic dose toxic symptoms arise. As in the case of other serous cavities, drugs are rapidly absorbed from the subarachnoid space and can thus directly affect the brain; when neurotropic drugs such as strychnine are administered by this route, in order to obtain the same effect as by other methods it is necessary to diminish the dose considerably. In the case of salvarsan, intravenously injected, the organotropic action is small and therefore the quantity injected may be increased in order to obtain a maximum parasitotropic effect. The conditions are, however, different in the subarachnoid space. Here the drug is highly organotropic, and the "*dosis maxima bene tolerata*" is so small that its parasitotropic effect is trivial.

We are, therefore, of opinion that the intrathecal injection of "salvarsanized serum," or of neosalvarsan in its present form, can have no permanent vogue.

## Conclusions.

The progressive character of "parasyphilitic" lesions is due to a continuation of the syphilitic process in spite of treatment, and not to a progressive primary degeneration of the neurons. The degeneration passively extends to the limits of the neuron, but does not actively spread to other neurons. Treatment is ineffective in resolving the inflammation because drugs in the blood-stream are unable to pass from the capillaries into the nervous substance in order to destroy the spirochætes. If by some method salvarsan succeeds in penetrating into the brain or cord, it produces such toxic symptoms as make its use impossible.

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## Publications Recently Received.

[*Notes on a book under this heading do not preclude a subsequent review.*]

*Archives of Neurology and Psychiatry from the Pathological Laboratory of the London County Asylums.* Edited by F. W. Mott, M.D., F.R.S. Vol. vi. 1914. Pp. 354 numbered consecutively, followed by a series of papers numbered individually. London: P. S. King, 1914.

This volume of these well-known Archives from the Claybury Laboratory opens with a revised version of Dr. Mott's introductory address to the Neurological Section of the International Medical Congress on "The Nature of Parasyphilis." The original report was sent in to the Congress and printed in February, 1913; between that date and the meeting in August, Noguchi discovered the spirochæte in the brain of patients with general paralysis, and other new work necessitated some modification of the original paper. Thus, in the present number of the Archives we have Dr. Mott's reasoned views in the light of modern knowledge. Drs. Candler and Mann follow with "The Wassermann Reaction in the Diagnosis of Mental Disorders" and Dr. Wootton has a short paper on the results of the Wassermann Reaction obtained in Asylum practice. Then comes Dr. Mott's address, given at the opening of the Psychiatrical Clinic at Johns Hopkins University, on the "Neuropathic Inheritance, especially in Relation to Insanity." Dr. White gives twenty-five pedigrees of insane persons; Dr. Wootton a number of family histories; Dr. Schuster considers "Hereditary Resemblance in the Fissures of the Cerebral Hemispheres," and Dr. Baines discusses some cases of insanity occurring during the involutional period of life. This is followed by Dr. Fortuny's paper on "Cortical Cell-Lamination of the Hemispheres of some Rodents." The volume concludes with a series of communications by various workers in the Claybury Laboratory to Sections of the Royal Society of Medicine.

*Ueber das Sinnesleben des Neugeborenen.* Von Dr. Silvio Canestrini, S. 104, mit 60 Figuren im Text und auf 1 Tafel. Berlin: Springer, 1913.

The author of this work attached a tambour to the fontanelle of babies of from 1 to 14 days old; he registered the changes in brain pulsation, associated with various conditions, on a curve together with the respiratory movements. Records were taken from the baby asleep and awake hungry and stilled, and

under the influence of various sense stimuli. Even on the first day after birth light caused a reaction, visible on the curves; some change almost always followed the stronger sounds, although no response occurred to the human voice or to the tuning-fork. As might be expected, gustatory stimuli produced a rapid and profound effect; sugar quieted the pulsations, but sour and bitter solutions produced irregular movements accompanied by cessation of the act of sucking. Olfactory tests caused little or no effect, whilst tactile and painful stimuli either evoked no result or produced the same effect as any state of displeasure.

*Das Zittern.* Von Dr. JOSEPH PELNAŘ, A. o. Professor an der bömischen Universität in Prag. Aus dem Tschechischen übersetzt von Dr. GUSTAVE MÜHLSTEIN. S. 258, mit 125 Textfiguren. Berlin: Springer, 1913.

When the author of this monograph was assistant to Professor Thomayer, he took graphic records from all patients with tremor whatever its cause. He hoped to be able to make a differential diagnosis by the rate and nature of the oscillations revealed by these curves; unfortunately this was not possible. He deals first with the records he obtained, beginning with physiological tremor and passing through the various intoxications to the neuroses. Then he considers organic nervous diseases such as disseminated sclerosis and Parkinson's disease. Tracings of the tremor in exophthalmic goitre are also given. He then passes on to consider the pathology of these tremors in the light of the literature of the subject and his own observations. This is the weakest part of the book, for he seems to be ignorant of much recent work; thus v. Monakow is not cited and the nucleus ruber is not mentioned.

*Traité Clinique et Médico-légal des Troubles Psychiques et Névrosiques Post-Traumatiques.* Par R. BENON, Médecin de l'Hospice Générale de Nantes. Pp. 449. Paris: Steinheil, 1913.

A number of excellent cases where a more or less grave neurosis followed injury are reported by the author, who attempts to classify them under the headings of "Dysthénies," "Dysthymies," "Dysphrénies." These correspond roughly to asthenic states, which include chronic mania, affective disturbances, such as anxiety, hypochondria and alterations of character, and lastly, the intellectual affections such as amnesia, Korsakoff's psychosis confusion and dementia. Unfortunately there is no index, and it is therefore difficult to find the way through this unfamiliar classification; but the cases are admirably described and are well worth perusal. Every chapter is followed by many references to similar instances in the literature, with a short summary of each.

*A Manual of Psychology.* By G. F. STOUT, M.A., LL.D. Third Edition. Revised and enlarged. Pp. 769. London: University Tutorial Press, 1913.

This well-known work has been almost completely rewritten and revised. It is in fact a new book, and far the best exposition in English of the purely psychological point of view. Everyone interested in the psychical side of his work should study it carefully in order to learn the aspect from which the psychologist looks upon many phenomena with which the neurologist is daily familiar. The book opens with three chapters on the scope, data and methods of psychology and the relation of body and mind. These are followed by a general analysis of the manner in which the conscious subject is related to its objects, with a particularly fine chapter on Attention as the essential form of all mental activity. Book II is devoted to sensation, which, although it suffers from a want of daily familiarity with the facts on which it is based, will act as a useful corrective to loose thinking. Amongst the subsequent chapters of this most interesting text-book we can only mention those on spacial perception, memory, language, ideas and images as particularly important in view of certain materialistic tendencies of neurological thought.

*Epidemic Infantile Paralysis.* By Professor PAUL H. RÖMER. Translated by H. RIDLEY PRENTICE, M.B. Pp. 208, with 57 illustrations in the text. London: Bale, Sons and Danielsson, 1913.

An excellent translation of the important monograph by Professor Römer on infantile paralysis, noticed in BRAIN, vol. xxxiv, p. 536. It contains an account of the fruits of the Nassau epidemic, and a description of the strains of infective material obtained from acute cases of the disease. Everyone interested in the pathology or epidemiology of poliomyelitis should have this book upon his shelves.

*General Paresis.* By Professor EMIL KRAEPELIN. Authorized English Translation by J. W. MOORE, M.D. (Nervous and Mental Disease Monograph Series, No 14.) Pp. 200. New York: Journal of Nervous and Mental Disease Publishing Company, 1913.

This is a chapter on dementia paralytica from Kraepelin's "Text-book of Psychiatry," translated into English to form a monograph. It gives a good systematic account of the disease as it appears from the point of view of the alienist, but contains little concerning those varieties seen by the neurologist. Kraepelin still holds that "paresis" is a true disease based upon a distinctive pathological process. The translation by Dr. Moore is excellent.

*Klinik der Nervenkrankheiten.* Von Dr. LEO JACOBSOHN. S. 488, mit 367 Abbildungen im Text und 4 Tafeln in Farbendruck. Berlin: Hirschwald, 1913.

The best feature of this book is the pictures, which are excellent and almost all original. The text, on the other hand, is commonplace, and contains no information that is not in every text-book of neurology; the subjects in which knowledge has advanced most of recent years are dealt with insufficiently. Localization of lesions in the spinal cord, disease of the brain-stem, optic thalamus, corpus striatum, and cortex cerebri are treated according to the ideas of ten years ago. Evidently the writer is not acquainted with recent French or English work.

*Affektstörungen.* Von Dr. LUDWIG FRANK. S. 399. Berlin: Springer, 1913.

This work, strongly under the influence of Freud and his followers, is based entirely on the author's patients treated by a combination of hypnosis and psychotherapy. Long and wearisome histories of cases are given revealing the author's naive psychology. There is no index.

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**EDITOR.**